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New Drugs 2015

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LEARNING OBJECTIVES

Upon completion of this module, the subscriber will be able to:

1. Name the therapeutic class for each new agent.
2. Describe the disease state for which each new agent is indicated.
3. Discuss the dosage form and route of administration for each new agent.
4. Describe adverse effects for each class of agent discussed.
5. List special considerations related to storage, preparation, and dispensing for each new agent.



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Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this module is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs. Always refer to changes in federal law and any applicable state laws.

New Drugs 2015

INTRODUCTION

Nearly 100 new drugs were approved in 2013 and 2014 for over 50 indications. Of these, 48% are administered orally or sublingually and 44% are administered by injection or infusion. The remaining 8% includes drug products that are administered by inhalation, into the ear, and topically.

This module is intended to provide a brief overview of each new drug, focusing on information important to pharmacy technicians in their roles of medication procurement, storage, preparation, packaging, and ancillary supplies. Rather than presenting each drug in alphabetical order, these products have been arranged by medical specialty and by condition, following an order often used when a patient is evaluated by a healthcare provider. A brief overview of the disease or condition for which this drug is used will be provided prior to drug discussion. It is hopeful that this arrangement by context will help the reader to understand and retain the new information presented. Branded and trademarked names are written in capitals and are included to help with recognition and understanding of drugs and products discussed. Where applicable, look-alike and sound-alike drug names have been included.¹

Otolaryngology or ENT (Ear/Nose/Throat Diseases)

Otitis Externa

Swimmer's ear or otitis externa is often caused by a bacterial infection of the external parts of the ear that include the outer ear and the ear canal. Symptoms may include pain, swelling, redness, and drainage from the ear. While not yet marketed at the time of writing this module, **finafloxacin** (XTORO, approved 12/17/14) is a suspension of a new quinolone antibiotic instilled into the ear to treat acute otitis externa. In clinical trials, it was found to be more effective to treat external ear infections caused by the organisms *Pseudomonas aeruginosa* or *Staphylococcus aureus* than a placebo solution without the active ingredient.² The usual dose is four drops into the affected ear twice daily for seven days.

Side effects include itching in the treated ear and nausea. Allergic reactions are possible in those who have hypersensitivity to other quinolones, including ciprofloxacin (CIPRO) and levofloxacin (LEVAQUIN). These ear drops are packaged in plastic bottles with a drop tip. The product should be stored at room temperature and protected from freezing. Prior to administration, the patient should hold the bottle in their hands for about two minutes to prevent instilling a cold solution into the ear.³ See **Table 1** (page 5).

Cardiology (Heart Disease)

Reduction of Thrombotic Cardiovascular Events

Vorapaxar (ZONTIVITY, approved 5/8/14) is the first in a new class of drugs that inhibits or prevents blood clotting. It is known as a protease-activated receptor-1 (PAR-1) blocker and works by decreasing platelets' ability to stick to each other to form a blood clot. By doing this, the drug decreases the risk of heart attack and stroke. In a large clinical trial, when used in combination with aspirin and/or clopidogrel (PLAVIX), and when compared to placebo, vorapaxar was found to decrease the combined risk of heart attack, stroke, death from a cardiovascular event, and coronary blood flow surgery. Vorapaxar, like other blood clotting inhibitors, increases the risk of bruising and life-threatening internal bleeding. Because of this, the drug must be dispensed with an FDA-approved Medication Guide that provides patient information about the benefits and risks of the drug.⁴ The dose is 2.08 mg by mouth daily and the drug is used in patients who have had a heart attack or who have peripheral arterial disease. It should not be used in patients with a history of stroke, transient ischemic attack (TIA), head bleed, or with active bleeding. Because there are many drug interactions, it is important that a pharmacist review the patient's medication profile at the time of each dispensing. The drug must be dispensed in its original bottle. It is stored at room temperature. The desiccant in the bottle should not be discarded and the bottle should be kept tightly closed to protect the tablets from moisture.^{5,6} See **Table 2** (page 5).

Pulmonology (Lung Disease)

Chronic Obstructive Pulmonary Disease

Chronic Obstructive Pulmonary Disease (COPD) is a common, progressive, inflammatory and obstructive lung disease made up of three subtypes: chronic bronchitis, emphysema, and chronic obstructive asthma. Symptoms include a chronic cough, shortness of breath, chest tightness, and increased phlegm production. It affects 32 million Americans and is a leading cause of death in the US. Smoking is to blame for an overwhelming majority of COPD. The goals of COPD treatment include improving lung function, decreasing symptoms, and improving patient function and quality of life. It is managed by smoking discontinuation, airway bronchodilators, inhaled corticosteroids, oxygen, vaccines and pulmonary rehabilitation.⁷ Two new drugs and three new inhaled products were approved in 2013 and 2014 to treat COPD.

Vilanterol is a long acting beta-adrenergic agonist (LABA) that relaxes airways (bronchodilator) and has been approved for use in COPD in two combination products. One is with the corticosteroid **fluticasone** (BREO ELLIPTA, approved 5/10/13) and the other is combined with the anticholinergic **umeclidinium** (ANORO ELLIPTA, approved 12/18/13). Both are used once daily (one inhalation) for the long term maintenance of COPD. BREO ELLIPTA, vilanterol with fluticasone, relaxes airways and decreases lung inflammation. In clinical trials, it was found to improve lung function and decrease exacerbations when compared to placebo. It should be noted that other marketed LABA/corticosteroid inhalers are administered twice daily. In 2015, BREO ELLIPTA was additionally approved to treat asthma. Inhalers are available in two strengths: 25 mcg vilanterol with 100 mcg fluticasone or 25 mcg vilanterol with 200 mcg fluticasone. Common adverse reactions include nasal congestion, upper respiratory tract infection, headache, cough, and oral candida infection (thrush). ANORO ELLIPTA, vilanterol with umeclidinium, relaxes airways, including large airways. In clinical trials, lung function was improved when compared to placebo. It is the first combination anticholinergic/LABA available in the US, and it is available as 25 mcg vilanterol with 62.5 mcg umeclidinium per inhalation. Common adverse reactions include nasal congestion, lower respiratory tract infection, muscle spasms, neck pain, and chest pain. Prescribing information for both vilanterol products includes a black box warning of increased risk for asthma-related deaths. ANORO ELLIPTA is not approved for use

in asthmatics. Both of these products should be kept in their sealed foil trays at room temperature until they are ready for use. They should be discarded six weeks after opening or when the counter indicates “0”. The inhalers are not reusable. FDA-approved Medication Guides for both of these products include illustrated instructions for use.^{8,9,10,11}

Olodaterol (STRIVERDI RESPIMAT, approved 7/31/14) is also a LABA and relaxes airways. It is indicated for the long-term control of COPD. In clinical trials, lung function was improved when compared to placebo. Olodaterol, like vilanterol-containing products, has a black box warning for increased risks of asthma-related deaths. Like ANORO ELLIPTA, it has also not been approved for use in asthma. The dose is two inhalations (2.5 mcg per inhalation) once daily. Common side effects include nasal congestion, upper respiratory tract infection, bronchitis, cough, dizziness, rash, back pain, and joint pain.¹² Because it is a long-acting product, olodaterol should not be used for acute (sudden onset) COPD symptoms. The aluminum cartridge can only be used with the product's inhaler. Once the doses contained in the cartridge have been completed, the inhaler engages a locking mechanism. Each inhaler should not be used for more than three months. The product should be stored at room temperature and should not be frozen. The FDA-approved Medication Guide includes illustrated instructions for patient use of the device.¹³ See **Table 3**.

Gastroenterology (Gastrointestinal Disease)

Ulcerative Colitis and Crohn's Disease

Inflammatory bowel disease (IBD) is thought to be caused by an immune response in the gastrointestinal tract. There are two types of IBD: ulcerative colitis and Crohn's disease. While ulcerative colitis is usually limited to the colon, Crohn's disease can affect any part of the gastrointestinal tract. Ulcerative colitis affects about 620,000 in the US and death due to the disease is the same as that of the general population. The goal of treatment is to prevent disease flares and to cause remission, and may include symptom treatment, surgery and medications. Medications used to treat ulcerative colitis include aminosalicylates, corticosteroids, immunomodulators, tumor necrosis factor (TNF) inhibitors, and most recently, an integrin receptor antagonist. Crohn's disease affects over 500,000 in the US

Table 1. New Drugs for Otolaryngology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Finafloxacin (XTORO) ^a <i>Approved 12/17/14</i>	0.3% Otic Suspension	0065-xxxx-xx ^b	5 mL fill in an 8 mL bottle (1)	Store at 2-25°C (36-77°F). Do not freeze.

^a XTORO (finafloxacin otic suspension) [package insert]. Alcon; November 2014.

^b At the time of this writing, XTORO has not yet been released to market.

Table 2. New Drugs for Cardiology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Vorapaxar (ZONTIVITY) ^a <i>Approved 5/8/14</i>	Oral tablet	0006-0351-31 0006-0351-54 0006-0351-48	2.08 mg yellow oval tablets (30) 2.08 mg yellow oval tablets (90) 2.08 mg yellow oval tablets, unit dosed (100) >> marked "351" and the Merck logo	Store at room temperature. Store in original package. Keep desiccant in bottle.

^a ZONTIVITY (vorapaxar) [package insert]. Merck & Co., Inc.; April 2015.

Table 3. New Drugs for Pulmonology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Fluticasone-vilanterol (BREO ELLIPTA) ^a <i>Approved 5/10/13</i>	Powder for oral inhalation	0173-0859-10 0173-0859-14 0173-0882-10 0173-0882-14	100/25 Double-foil strips (2x30 blisters) 100/25 Double-foil strips (2x14 blisters) 200/25 Double-foil strips (2x30 blisters) 200/25 Double-foil strips (2x14 blisters) >> light grey and pale blue plastic inhaler	Store at room temperature. Protect from heat and sunlight. Protect from moisture.
Olodaterol (STRIVERDI RESPIMAT) ^b <i>Approved 7/31/14</i>	Inhalation spray	0597-0192-61 0597-0192-31	60 metered actuations (1) 28 metered actuations (1) >> aluminum cylinder cartridge >> grey inhaler with dose indicator	Store at room temperature. Avoid freezing.
Umeclidinium-vilanterol (ANORO ELLIPTA) ^c <i>Approved 12/18/13</i>	Powder for oral inhalation	0173-0869-10 0173-0869 06	Double-foil strips (2x30 blisters) Double-foil strips (2x7 blisters) >> light grey and pale red plastic inhaler	Store at room temperature. Store in unopened protective tray. Protect from heat and sunlight.

^a BREO ELLIPTA (fluticasone furoate and vilanterol inhalation powder) [package insert]. GlaxoSmithKline; April 2015.

^b STRIVERDI RESPIMAT (olodaterol inhalation spray) [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc.; July 2014.

^c ANORO ELLIPTA (umeclidinium and vilanterol inhalation powder) [package insert]. GlaxoSmithKline; December 2013

and death from the disease is greater than that of the general population. As in ulcerative colitis, the goal of treatment is to prevent disease flares and to cause remission. Medications used to treat Crohn's disease include corticosteroids, immunomodulators, TNF inhibitors, and now, an integrin receptor antagonist.¹⁴

Vedolizumab (ENTYVIO, approved 5/19/14) is a humanized monoclonal antibody that is indicated for moderate to severe refractory ulcerative colitis or Crohn's disease in adults. It is an integrin receptor antagonist that inhibits (prevents) the migration of white blood cells into intestinal tissue. The drug works in the gastrointestinal tract only, in contrast to the integrin receptor antagonist, natalizumab (TYSABRI), which inhibits migration of white blood cells across the blood-brain barrier and is used in the treatment of multiple sclerosis. Clinical trials for both ulcerative colitis and Crohn's disease showed an improved clinical response and a higher rate of remission over placebo. There are currently no trials that compare vedolizumab with other inflammatory bowel disease treatments, and safety has not been established with simultaneous administration of vedolizumab with other biologicals. Adverse effects may include allergic reactions, infection, liver injury, nasal congestion, headache, nausea, fever, upper respiratory tract infection, fatigue, cough, back and limb pain, rash, and itching. Vaccinations should be administered before vedolizumab is initiated. The drug is stored in the refrigerator, reconstituted with sterile water, and further diluted in 250 mL normal saline. It may take up to 20 minutes to reconstitute. The diluted product

must be used within 4 hours because it contains no preservatives. Since it is a protein, it should not be shaken. The 300 mg dose is administered intravenously over 30 minutes at weeks 0, 2, 6, and then every eight weeks. It is an expensive drug, with a wholesale acquisition cost (WAC) of nearly \$5,000 per 8-week treatment.^{15,16}

Opioid-induced Constipation

Constipation and difficult bowel movements, caused by slowed gastrointestinal motility, is a common side effect of long term pain management with opioids (ex. hydrocodone, codeine, morphine, etc.). **Naloxegol** (MOVANTIK, approved 9/16/14) is an opioid antagonist that lessens opioid effects on the gastrointestinal tract without blocking their affect on alleviating pain. Clinical trials showed that while on naloxegol, the number of bowel movements per week increased as compared with placebo.¹⁷ It is a C-II controlled substance. Side effects include abdominal pain, diarrhea, nausea, headache, and increased gas. The drug is available as a tablet in two strengths (12.5 mg and 25 mg) and is taken once daily by mouth in the morning on an empty stomach. The tablets should not be crushed. Eating grapefruit or drinking grapefruit juice should be avoided when on naloxegol. It should not be used in patients who have or are at risk of bowel obstruction, nor should it be used by patients taking clarithromycin or ketoconazole due to drug interaction (more drug interactions exist). Patients should not be taking laxatives before starting naloxegol, and it should be stopped if the patient is no longer on an opioid pain medication.¹⁸

Table 4. New Drugs for Gastroenterology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Naloxegol (MOVANTIK) ^a <i>Approved 9/16/14</i>	Oral tablet	0310-1969-30 0310-1969-90 0310-1969-39 0310-1970-30 0310-1970-90 0310-1970-39	12.5 mg mauve oval tablets (30) 12.5 mg mauve oval tablets (90) 12.5 mg unit-dosed mauve oval tablets (100) 25 mg mauve oval tablets (30) 25 mg mauve oval tablets (90) 25 mg unit-dosed mauve oval tablets (100) >> marked "nGL" and "12.5 or "25"	Store at room temperature.
Netupitant/palonosetron (AKYNZEO) ^b <i>Approved 10/10/14</i>	Oral capsule	62856-796-01	300 mg netupitant/0.5 mg palonosetron (1) >> white and caramel gelatin capsule >> marked "HE1"	Store at room temperature.
Vedolizumab (ENTYVIO) ^c <i>Approved 5/20/14</i>	Lyophilized powder for intravenous infusion	64764-300-20	300 mg single-dose vial (1)	Refrigerate. Protect from light.

^a MOVANTIK (naloxegol) [package insert]. AstraZeneca Pharmaceuticals LP; September 2014

^b AKYNZEO (netupitant and palonosetron) [package insert]. Eisai, Inc.; October 2014

^c ENTYVIO (vedolizumab) [package insert]. Takeda Pharmaceuticals America, Inc.; May 2014

Chemotherapy-induced Nausea & Vomiting

Nausea and vomiting often accompany anti-cancer treatments; therefore, antiemetics are usually ordered to prevent nausea and vomiting when chemotherapy is started and for nausea and vomiting that can develop later. **Netupitant** is a substance P/neurokinin-1 receptor antagonist that has been combined with **palonosetron**, a serotonin receptor antagonist in a first combination of these two classes of drugs to treat acute and delayed chemotherapy-induced nausea and vomiting (CINV). Palonosetron (ALOXI) has been available in its oral form since 2003. The combination product (AKYNZEO, approved 10/10/14) was evaluated in two trials and showed that significantly more patients did not experience vomiting during either the acute or the delayed phase following chemotherapy, as compared with palonosetron alone. The most common side effects are headache, weakness, fatigue, indigestion, and constipation.¹⁹ The usual dose is one capsule (300 mg netupitant and 0.5 mg palonosetron) given one hour before starting chemotherapy. It can be taken with or without food. Patients who receive chemotherapy that is known to cause a high degree of nausea and vomiting should also be given dexamethasone prior to treatment. This new combination therapy appears to be similar to other multi-drug anti-nausea regimens used in standard protocols. This combination therapy should be avoided in patients with severe liver or kidney impairment.²⁰ See **Table 4**.

Women's Health

Pregnancy

Doxylamine succinate and pyridoxine hydrochloride (DICLEGIS, approved 4/8/13) is a “new” delayed-release combination product for severe nausea and vomiting

related to pregnancy, otherwise known as hyperemesis gravidarum. It combines the antihistamine doxylamine and vitamin B6, also known as pyridoxine. In clinical trials, the combination showed a decrease in nausea and vomiting in pregnant women, as compared to placebo. The most significant side effect is drowsiness. For those who have been working in pharmacy for a very long time, this new dosage form has the same components as BENDECTIN, which was taken off the US market in 1983 due to unfounded allegations of birth defects. Interestingly, the older product continued to be available in Canada. The product should be protected from moisture, with the bottle tightly sealed and the desiccant kept in place. When treating nausea due to pregnancy, it may be useful for the patient to first try avoiding foods and odors that trigger nausea; to eat smaller, more frequent meals; and to try medications as a last resort. DICLEGIS is taken daily, two tablets at bedtime, on an empty stomach. If symptoms are not controlled, the dose can be increased to a maximum of four tablets daily, one in the morning, one mid-day, and two at bedtime. As the pregnancy progresses after the third trimester, nausea and vomiting usually subside, and continuation of DICLEGIS should be re-evaluated.^{21,22,23} Do not confuse pyridoxine with PYRIDIDIUM (phenazopyridine).¹

Menopause

In menopause, decreasing estrogen levels cause vaginal tissues to become more thin, dry, and fragile. **Ospemifene** (OSPHENA, approved 2/26/13) is an estrogen-like drug that improves the integrity of vaginal tissues, thereby decreasing intercourse pain during menopause. In clinical trials, postmenopausal women treated with ospemifene reported a significant decrease in pain during intercourse than those who received placebo. The package insert includes a black box warning about the risk of endometrial

Table 5. New Drugs for Women's Health

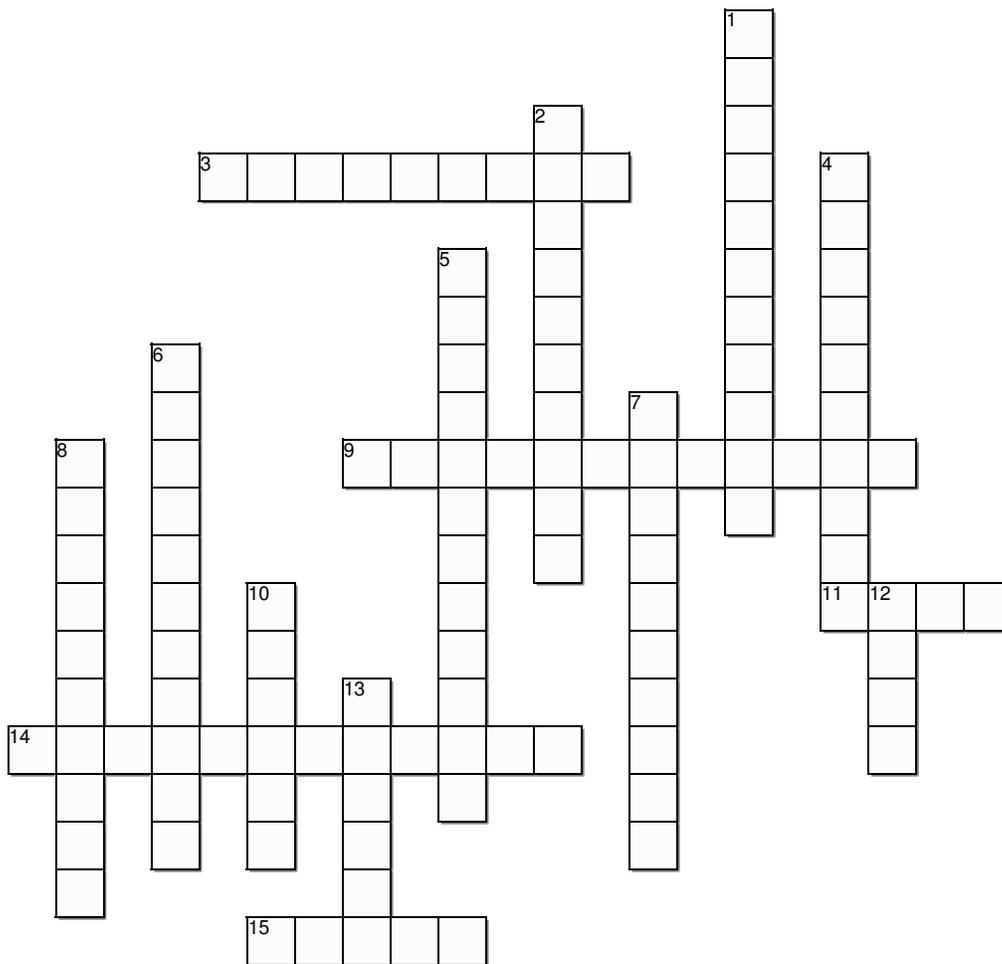
Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Doxylamine succinate & pyridoxine hydrochloride (DICLEGIS) ^a Approved 4/8/13	Delayed-release oral tablets	55494-100-10	10 mg doxylamine/10 mg pyridoxine white round tablets (100) >> marked with a pink image of a pregnant woman	Store at room temperature. Protect from moisture. Do not remove desiccant.
Ospemifene (OSPHENA) ^b Approved 2/26/13	Oral tablet	59630-580-10 59630-580-30	60 mg off-white oval tablets (100) 60 mg off-white oval tablets blister pack (2x15) >> marked with “60” on one side	Store at room temperature.

^a DICLEGIS (doxylamine succinate and pyridoxine hydrochloride) [package insert]. Duchesnay USA, Inc.; April 2013

^b OSPHENA (ospemifene) [package insert]. Shionogi, Inc.; February 2015

New Drugs Crossword Puzzle A

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

3. Item that should not be removed from DICLEGIS' original packaging.
9. ENTYVIO should be stored in the _____.
11. BREO ELLIPTA and ANORO ELLIPTA indication.
14. MOVANTIK is indicated for opioid-induced _____.
15. Sterile _____ is used to reconstitute ENTYVIO.

Down

1. The generic name for ENTYVIO.
2. The route of administration for BREO ELLIPTA and ANORO ELLIPTA.
4. XTORO belongs to which drug class?
5. The generic name for XTORO.
6. DICLEGIS is indicated for _____ gravidarum.
7. _____ and palonosetron (AKYNZEO) is indicated in chemotherapy-induced nausea and vomiting.
8. ENTYVIO is a(n) _____ antibody.
10. Once reconstituted, _____ is used to dilute ENTYVIO.
12. The route of administration for XTORO.
13. MOVANTIK dosage form.

Answers on page 54.

cancer, stroke, and deep-vein thrombosis. Long-term safety has not been established with this treatment. Side effects include hot flashes, vaginal discharge, spasms, and increased sweating. OSPHENA 60 mg tablets are stored at room temperature and taken once daily by mouth with food.^{24,25} See Table 5 (page 7).

Neurology (Brain Disease)

Insomnia

Suvorexant (BELSOMRA, approved 8/13/14) is the first orexin antagonist to treat insomnia, the inability to fall or to stay asleep. When a person is awake, orexin neurons are active and when a person is asleep, these neurons are silent. In clinical trials, individuals who took suvorexant fell asleep faster and were awake less than those taking a placebo. The most common side effects are drowsiness and impairment in the ability to drive the next day. As with other medications that induce sleep, individuals taking suvorexant are at risk of unknowingly performing tasks or activities while not awake. Drug interactions include other depressant drugs, or those that decrease the metabolism of suvorexant, including grapefruit juice. The lowest effective dose is taken by mouth once nightly, 30 minutes before bedtime and at least 7 hours before planned awakening. The maximum daily dose is 20 mg. The tablets are dispensed in the original packaging to protect it from light and moisture. Due to the potential for dependence or abuse, suvorexant is a Schedule-IV controlled substance.^{26,27,28}

Seizures

Partial seizures are the most common type of epileptic seizure. These seizures start in a localized area of the brain. Annually, about 200,000 new cases of epilepsy are diagnosed. The incidence of epilepsy follows a U-shaped curve, being higher in infants and also in older persons, aged 60 to 70 years old or older. When compared with the general population, death is about 2 times higher in those with epilepsy. Treatment options include anticonvulsants, also known as antiepileptics, and surgery. Partial onset seizures are usually treated with more than one antiepileptic.²⁹

Eslicarbazepine (APTIOM, approved 11/8/13) is a pro-drug, meaning it is converted or metabolized into its active form by the body. Eslicarbazepine is similar to

oxcarbazepine (TRILEPTAL; OXTELLAR XR) and carbamazepine (TEGRETOL; CARBATROL; EQUETRO). Clinical trials showed that eslicarbazepine was more effective in reducing the frequency of partial seizures than placebo. Studies have not compared eslicarbazepine with oxcarbazepine or carbamazepine. Side effects include dizziness, drowsiness, nausea, headache, double vision, vomiting, fatigue, and loss of coordination. Adverse effects can also include serious skin reactions and low blood sodium. Patients should not drive or operate machinery until they are familiar with how the drug affects them. Antiepileptic drugs may cause suicidal thoughts and patients should contact their prescriber if they experience any unusual change in mood or behavior. The starting dose of eslicarbazepine is a 400 mg tablet daily, increasing one week later to 800 mg daily. The maximum dose is 1,200 mg daily. Lower doses are given to patients with decreased kidney function. Eslicarbazepine should be discontinued slowly to minimize worsening of seizures. The drug can decrease the efficacy of hormone contraceptives.^{30,31,32}

Multiple Sclerosis

Multiple sclerosis (MS) is a disease in which the central nervous system is attacked and damaged by the immune system, forming plaques. The location of these plaques in the brain, spinal cord, and optic nerve governs the way in which the disease expresses itself. Usually, MS follows a relapsing-remitting pattern, in which symptoms flare and then subside. About 400,000 people in the US are affected by MS, according to the National Multiple Sclerosis Society (NMSS). More women than men are affected. If not treated, people with MS develop disabilities which significantly affect their activities of daily living. Death is usually a result of complications rather than MS itself. Treatment options include medications that address the immune disorder and those that address symptoms.³³ Two drugs were approved for MS in 2013 and 2014, one oral, and one injectable.

Dimethyl fumarate (TECFIDERA, approved 3/27/13) is indicated for adults with relapsing MS and is the third oral drug approved for MS. While it is thought that dimethyl fumarate acts as an anti-oxidant, it is not known how it works against MS. Clinical trials showed that patients treated with dimethyl fumarate had fewer relapses than those taking a placebo. Within one of the trials, worsening of disability was less frequent in patients treated with dimethyl fumarate than with placebo. Ad-

Table 6. New Drugs for Neurology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Dimethyl fumarate (TECFIDERA) ^a <i>Approved 3/27/13</i>	Delayed-release oral capsules	64406-007-03	120 mg green/white capsules (14, 7-days)	Store at room temperature. Protect from light. Store in original container. Once opened, discard after 90 days.
		64406-005-01	240 mg green capsules (46, 23-days)	
		64406-006-02	120 mg green/white capsules (14, 7-days)	
			240 mg green capsules (60, 30-days) >> marked “BG-12 120 mg” in black >> marked “BG-12 240 mg” in black	
Eslicarbazepine (APTIOM) ^b <i>Approved 11/8/13</i>	Oral tablets	63402-202-30	200 mg white oblong scored tablet (30)	Store at room temperature.
		63402-204-30	400 mg white circular tablet (30)	
		63402-206-60	600 mg white oblong scored tablet (60)	
		63402-206-90	600 mg white oblong scored tablet (90)	
		63402-208-30	800 mg white oblong scored tablet (30)	
		63402-208-90	800 mg white oblong scored tablet (90) >> marked according to dose as “ESL 200”, “ESL 400”, “ESL 600”, or “ESL 800”	
Peginterferon beta-1A (PLEGRIDY) ^c <i>Approved 8/15/14</i>	Subcutaneous injection	64406-011-01	125 mcg in 0.5 mL pre-filled pens (2)	Refrigerate. May be stored at room temperature for 30 days. Warm to room temperature prior to injection. Protect from light.
		64406-012-01	63 mcg in 0.5 mL pre-filled pen (1) and 94 mcg in 0.5 mL pre-filled pen (1)	
		64406-015-01	125 mcg in 0.5 mL pre-filled syringe (2)	
		64406-016-01	63 mcg in 0.5 mL pre-filled syringe (1) and 94 mcg in 0.5 mL pre-filled syringe (1)	
Suvorexant (BELSOMRA) ^d <i>Approved 8/13/14</i>	Oral tablets	0006-0005-30	5 mg yellow round tablet unit dose (30) >> marked “5” on one side	Controlled substance, C-IV Store at room temperature. Protect from light and moisture. Store in original package until use.
		0006-0033-30	10 mg green round tablet unit dose (30) >> marked “33” on one side	
		0006-0325-30	15 mg white oval tablet unit dose (30) >> marked with Merck logo and “325”	
		0006-0335-30	20 mg white round tablet unit dose (30) >> marked with Merck logo and “335”	

^a TECFIDERA (dimethyl fumarate) [package insert]. Biogen Idec, Inc.; April 2015.

^b APTIOM (eslicarbazepine) [package insert]. Sunovion Pharmaceuticals, Inc.; August 2015.

^c PLEGRIDY (peginterferon beta-1A) [package insert]. Biogen Idec, Inc.; August 2014.

^d BELSOMRA (suvorexant) [package insert]. Merck & Co., Inc.; October 2014.

verse effects include decreasing white blood cells, flushing, nausea, vomiting, and diarrhea. It is not known to interact with other drugs. Dimethyl fumarate is started at a dose of 120 mg twice daily for a week, followed by the maintenance dosing of 240 mg twice daily. It can be given with or without food, but flushing may be decreased if it is taken with food. Capsules are delayed release, so they should be swallowed whole and should not be crushed, chewed, or sprinkled on food. Because it affects white blood cell counts, prescribers should take a baseline blood count before the patient is started on therapy. Dimethyl fumarate should be stored in its original container to protect the capsules from light. Once the original container is opened, it should be discarded after 90 days. The WAC for one year’s treatment is

about \$54,000 which is less than fingolimod (GILENYA), but more than teriflunomide (AUBAGIO).^{34,35,36}

Peginterferon beta-1a (PLEGRIDY, approved 8/15/14) is a pegylated form of interferon beta-1a indicated for the treatment of relapsing MS in adults. Pegylation means that a chain of polyethylene glycol is fused to the original interferon beta-1a molecule, thereby making it much longer acting than the original. Like the original, peginterferon beta-1a is thought to work by improving immune cell activity. Clinical trials showed that annualized relapse rates, expanded disability status scale, and brain lesions on MRI were significantly lower than with placebo. Warnings include liver injury, depression, sui-

cide, seizure, and decreased blood counts. Adverse effects include injection site reactions, flu-like symptoms, fever, headache, muscle aches, and chills. The dosing regimen is 63 mcg subcutaneously on day 1, 94 mcg subcutaneously on day 15, 125 mcg subcutaneously on day 29 and then every two weeks thereafter. A starter pack is available for dose titration. To decrease flu-like symptoms, the patient may take an analgesic/antipyretic such as acetaminophen prior to injection. This injection contains no preservatives, should be refrigerated, not frozen, and protected from light. The prefilled syringes should be left at room temperature for 30 minutes to warm prior to injection. No other method of warming may be used. If refrigeration is not available, peginterferon beta-1a may be stored at room temperature for up to 30 days. The annual WAC is about \$65,000, the same as that for 3-times weekly interferon beta-1a AVONEX, and less than that for REBIF. There are no clinical studies comparing the pegylated form of interferon beta-1a to the original. After receiving proper training, most patients can self-administer this therapy.^{37,38} Do not confuse the MS drug peginterferon beta-1a with hepatitis C virus (HCV) drugs peginterferon alfa-2a (PEGASYS) and peginterferon alfa-2b (PEGINTRON). See **Table 6**.

Psychiatry (Mental Disease)

Major Depression

While the specific cause of depression is not known, it is thought that serotonin, norepinephrine, and dopamine levels in the central nervous system play a role. The lifetime incidence of major depressive disorder is about 20% in females and 12% in males. It plays a significant role in more than half of suicide attempts and its death rate is greater than 15%. Treatment of depression includes psychotherapy and medication. Medications used in depression include selective serotonin reuptake inhibitors (SSRIs such as fluoxetine), selective serotonin/norepinephrine reuptake inhibitors (SNRIs such as venlafaxine), atypical antidepressants, tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs).³⁹

Levomilnacipran (FETZIMA, approved 7/25/13) is a SNRI and is similar in structure to milnacipran (SAVELLA, approved in 2009 for fibromyalgia). Clinical trials found that patients treated with levomilnacipran showed better improvement on a depression rating score than those treated with placebo. Side effects include nausea, constipation, increased heart rate, palpitations, vomiting, erectile dysfunction, increased blood pressure, and

increased risk of bleeding if taken with aspirin or non-steroidal anti-inflammatory drugs (NSAIDs). Enzyme inhibitors like ketoconazole (NIZORAL) increase blood levels of levomilnacipran, requiring a reduction in dose. The starting dose is 20 mg daily by mouth for 2 days, then 40 mg daily. Depending on patient response, the dose may be increased by 40 mg every two or more days up to a maximum of 120 mg daily. The extended release capsules should be taken whole, not opened, chewed, or crushed. It can be taken with or without meals. Discontinuation should be gradual.⁴⁰ Do not confuse FETZIMA with the diabetes drug FARXIGA (dapagliflozin).¹

Vortioxetine (BRINTELLIX, approved 9/30/13) is a “multimodal” serotonergic that primarily works like a SSRI. In clinical trials, patients had significantly lowered depression rating scores and a longer time to depressive episode recurrence than placebo. Common side effects include nausea, vomiting, and constipation. The starting dose is 10 mg by mouth daily, which is then either increased to 20 mg daily or decreased to 5 mg daily, depending on patient response. The tablets can be taken with or without meals. While vortioxetine can be discontinued abruptly, it is recommended that doses of 15 to 20 mg per day be reduced to 10 mg daily for one week before discontinuation.⁴¹ Do not confuse BRINTELLIX with the cardiac drug BRILINTA (ticagrelor).¹

Both levomilnacipran and vortioxetine have black box warnings for suicidal thoughts. Patients should contact their prescriber if they experience any unusual change in mood or behavior. Neither drug should be given to patients who are taking MAOIs. The WAC for both of these new antidepressants is about \$200 monthly, while that of a generic SSRI or SNRI is about \$20 monthly.^{42,43} See **Table 7 (page 12)**.

Rheumatology (Joint/Immune Disease)

Psoriatic Arthritis

Psoriatic arthritis is an inflammatory disease that develops in about 5% of patients with psoriasis. It was not seen as a different form of arthritis until the 1960s. Symptoms include joint pain, stiffness, and swelling. Treatment has included corticosteroids, TNF blockers, and an interleukin antagonist. **Apremilast** (OTEZLA, approved 3/21/14) is the first phosphodiesterase type-4 (PDE4) inhibitor for adults with psoriatic arthritis. It is thought to work by decreasing the inflammatory response. In clinical trials it was found to

Table 7. New Drugs for Psychiatry

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description, “Imprint” (Quantity)	Storage Conditions
Levomilnacipran (FETZIMA) ^a <i>Approved 7/25/13</i>	Extended-release oral capsules	0456-2220-30	20 mg yellow/white capsule (30)	Store at room temperature.
		0456-2220-63	20 mg yellow/white capsule (10x10 UD) >> marked with black “FL” and “20”	
		0456-2240-30	40 mg yellow/yellow capsule (30)	
		0456-2240-90	40 mg yellow/yellow capsule (90)	
		0446-2240-63	40 mg yellow/yellow capsule (10x10 UD) >> marked with black “FL” and “40”	
		0456-2280-30	80 mg pink/white capsule (30)	
		0456-2280-90	80 mg pink/white capsule (90)	
		0456-2280-63	80 mg pink/white capsule (10x10 UD) >> marked with black “FL” and “80”	
		0456-2212-30	120 mg pink/pink capsule (30)	
		0456-2212-90	120 mg pink/pink capsule (90)	
		0456-2212-63	120 mg pink/pink capsule (10/10 UD) >> marked with black “FL” and “120”	
		0456-2202-28	20 mg (2) and 40 mg (26) titration pack	
		Vortioxetine (BRINTELLIX) ^b <i>Approved 9/30/13</i>	Oral tablet	
64764-550-90	5 mg pink oblong tapered tablet (90)			
64764-550-77	5 mg pink oblong tapered tablet (500) >> marked “5” and “TL”			
64764-560-30	10 mg yellow oblong tapered tablet (30)			
64764-560-90	10 mg yellow oblong tapered tablet (90)			
64764-560-77	10 mg yellow oblong tapered tablet (500) >> marked “10” and “TL”			
64764-570-30	15 mg orange oblong tapered tablet (30)			
64764-570-90	15 mg orange oblong tapered tablet (90)			
64764-570-77	15 mg orange oblong tapered tablet (500) >> marked “15” and “TL”			
64764-580-30	20 mg red oblong tapered tablet (30)			
64764-580-90	20 mg red oblong tapered tablet (90)			
64764-580-77	20 mg red oblong tapered tablet (500) >> marked “20” and “TL”			

^a FETZIMA (levomilnacipran) [package insert]. Forest Pharmaceuticals, Inc.; July 2014.

^b BRINTELLIX (vortioxetine) [package insert]. Takeda Pharmaceuticals America, Inc.; July 2014.

have a better ACR20 (20% American College of Rheumatology) response than placebo. Unfortunately, the ACR50 and ACR70 responses were not significantly different than placebo. There are no studies in which apremilast has been compared with other antiarthritic treatments. Common side effects include diarrhea, nausea and headache. The drug can increase the risk of depression and has resulted in weight loss. Drug interactions occur with enzyme inducers (e.g., rifampin), resulting in decreased effect. The starting dose for patients with normal kidney function is 10 mg by mouth twice daily, increased over 6 days to 30 mg twice daily, and can be taken with or without food. Patients with kid-

ney dysfunction should be dosed once daily. A starter pack is available to assist with dose titration. The tablets should not be crushed, chewed, or split. The WAC is almost \$2,000 for a month’s treatment.^{44,45,46} See **Table 8**.

Immunology (Immune/Allergic Disease)

Allergic Rhinitis

Known as hay fever, allergic rhinitis symptoms include sneezing, nasal itching, congestion, tearing, and a run-

Table 8. New Drugs for Rheumatology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Apremilast (OTEZLA) ^a <i>Approved 3/21/14</i>	Oral tablets	59572-630-06 59572-630-27 59572-630-28	30 mg beige diamond shaped tablet (60) 30 mg beige diamond shaped tablet (2x14) 10 mg pink diamond shaped tablet (4) 20 mg brown diamond shaped tablet (4) 30 mg beige diamond shaped tablet (19) >> 10 mg tablet is marked "APR" and "10"; 20 mg tablet is marked "APR" and "20"; 30 mg tablet is marked "APR" and "30"	Store below 30°C (86°F).

^a OTEZLA (apremilast) [package insert]. Celgene Corporation.; March 2014.

ny nose. While it is not life-threatening, it affects about 30 million Americans and causes significant morbidity (being diseased or unhealthy). The cause is often due to allergy to grass pollen and ragweed. Three allergen extracts have been approved in 2014 as a sublingual alternative to subcutaneous allergy injections administered in a physician's office. **Grass pollen extract** (ORALAIR, approved 4/2/14 and GRASTEK, approved 4/11/14) and **Ragweed pollen extract** (RAGWITEK, approved 4/17/14) are derived from grasses and ragweed. Clinical trials of ORALAIR and GRASTEK in children and adults and of RAGWITEK in adults showed that symptom scores were decreased if started three to four months prior to and during the pollen season, as compared with placebo. ORALAIR is made up of sweet vernal, orchard perennial rye, timothy, and Kentucky blue grass pollen; GRASTEK contains timothy grass pollen; and RAGWITEK includes short ragweed pollen. Most common adverse effects during initial treatment include mouth, ear, and tongue itching. These products should not be used in patients with severe asthma, or immediately after tooth extraction. Therapy should begin three to four months (depending on product) before the start of pollen season. Because anaphylaxis has occurred on rare occasion, patients should have injectable epinephrine available. The first dose should be administered in a healthcare setting, with the patient observed for at least 30 minutes. Continued doses can be administered in the home. A sublingual tablet is placed under the tongue daily, allowing it to dissolve for at least one minute without swallowing. The patient shouldn't eat or drink until at least 5 minutes after the dose has been taken. After handling tablets, the patient should wash their hands. It is not known how long therapy should continue, nor how it compares to subcutaneous allergy injections.^{47,48,49,50,51} See **Table 9** (page 14).

Endocrinology (Endocrine and Hormonal Disorders)

Diabetes

In 2011, the CDC estimated that 26 million Americans have diabetes, and that 79 million are pre-diabetic and at risk of developing diabetes. This means that one-third of the US population knows they are affected by, or are at risk of, diabetes. Unfortunately, these statistics don't include the roughly 25% of the population that do not even know they have diabetes! There are two types of diabetes, type 1 and type 2. In type 1 diabetes, the pancreas does not produce insulin. Insulin is the hormone that regulates the amount of sugar in the blood and the amount brought into cells to provide them with energy. In type 2 diabetes, the body, over time, becomes resistant to insulin. High blood sugar levels lead to many serious complications, including heart disease, kidney damage, nerve damage, and blindness. In 2002, the cost of health care per diabetic was estimated to be \$13,250, while it was only \$2,500 for those without the condition. The goals of treating diabetes are to maintain appropriate blood sugar and hemoglobin A1c (HbA1c) levels. HbA1c is a marker on hemoglobin that shows exposure to high blood sugar levels over time. Treatment options for diabetes include education, diet, exercise, and medications.⁵²

Alogliptin (NESINA, approved 1/25/13) is the fourth dipeptidyl peptidase-4 (DPP-4) inhibitor to be approved for type 2 diabetes. Sitagliptin (JANUVIA) was approved in 2006, saxagliptin (ONGLYZA) in 2009, and linagliptin (TRADJENTA) in 2011. This class of anti-diabetic drugs is also known as "gliptins." By inhibiting DPP-4, gliptins allow incretin hormones to support insulin release and decrease glucagon levels, thereby decreasing blood glu-

Table 9. New Drugs for Immunology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Grass pollens extract (ORALAIR) ^a <i>Approved 4/2/14</i>	Allergen extract sublingual tablets	59617-0020-1	Child/Adolescent Sample Kit 100 IR Starter Pack (1) 300 IR Sample Pack (2)	Store at room temperature. Protect from moisture.
		59617-0026-1	Adult Sample Kit 300 IR Starter Pack (1) 300 IR Sample Pack (2)	
		59617-0010-1	Child/Adolescent Starter Pack 100 IR tablets (3) blister pack	
		59617-0016-1	Adult Starter Pack 300 IR tablets (3) blister pack	
		59617-0015-3	Sample Pack 300 IR tablets (3) blister pack	
		59617-0015-2	Commercial Pack 300 IR tablets (30) blister pack	
Grass pollen extract (GRASTEK) ^b <i>Approved 4/11/14</i>	Allergen extract sublingual tablets	0006-4229-30	2800 BAU white circular tablets (3x10) blister packs >> marked with round detail on one side	Store at room temperature. Protect from moisture.
Ragweed pollen extract (RAGWITEK) ^c <i>Approved 4/17/14</i>	Allergen extract sublingual tablets	0006-5420-30	12 Amb a 1-U white circular tablets (3x10)	Store at room temperature.
		0006-5420-54	12 Amb a 1-U white circular tablets (9x10) >> marked with a double hexagon	Protect from moisture.

^a ORALAIR (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass mixed pollens allergen extract) [package insert]. GREER Laboratories, Inc.; October 2014.

^b GRASTEK (Timothy Grass pollen allergen extract) [package insert], Merck & Co., Inc.; April 2014

^c RAGWITEK (Short Ragweed pollen allergen extract) [package insert]. Merck & Co., Inc.; June 2014.

cause. In addition to being approved as a single-ingredient product, it is also available in combination with metformin (KAZANO, approved 1/25/13) and with pioglitazone (OSENI, approved 1/25/13). In clinical trials, all three alogliptin products were shown to significantly decrease HbA1c levels in comparison to placebo or therapy with one drug of the combination products. The usual dose for NESINA is 25 mg once daily, for KAZANO is 12.5 mg alogliptin with 500-1000 mg metformin taken orally twice daily with food, and for OSENI is 25 mg alogliptin with 15-45 mg once daily. Lower doses may need to be given in decreased kidney function and in older people because of their decreased kidney function. Acute pancreatitis has been associated with DPP-4 inhibitors, low blood glucose can occur, as well as severe allergic reactions. Because KAZANO includes metformin, the package insert has a black box warning for increased risk of lactic acidosis, and because OSENI includes pioglitazone, there is a black box warning for increased risk of heart failure. Common side effects for NESINA, KAZANO, and OSENI include headache, runny nose and upper respiratory tract infection. Additionally, KAZANO may

cause diarrhea and high blood pressure; while OSENI or KAZANO may cause sore throat and back pain. The FDA is requiring post-market clinical trials of these products related to cardiac, liver, hypersensitivity, pancreatitis and pediatric safety. A month's treatment costs about \$250 (WAC) for any of these alogliptin products.^{53,54,55,56,57}

A new class of anti-diabetic drugs was approved by the FDA in 2013, known as sodium-glucose-co-transporter 2 (SGLT2) inhibitors. These drugs decrease blood sugar by increasing kidney excretion of glucose. Three SGLT2 inhibitors were approved in 2013 and 2014, **canagliflozin** (INVOKANA, approved 3/29/13), **dapagliflozin** (FARXIGA, approved 1/8/14), and **empagliflozin** (JARDIANCE, approved 8/1/2014). All three of these new drugs were shown to improve HbA1c and fasting blood glucose in clinical trials involving patients with type 2 diabetes, tested as single treatments or in combination with other anti-diabetic agents. When used with other agents, hypoglycemia may occur. SGLT2 inhibitors should not be used in patients with type 1 diabetes or in those with severe kidney disease. The most common side effects of

this new drug class include genital yeast infections and urinary tract infections. In addition, canagliflozin and dapagliflozin may cause low blood pressure when standing up, causing dizziness or fainting during the first few months taking the drug. The FDA is requiring several post-market clinical trials for each of these drugs. Each of them is to be evaluated for cardiac and pediatric safety. Canagliflozin and dapagliflozin are to be studied in cardiac, cancer risk, severe hypersensitivity, liver, and pregnancy safety; while canagliflozin must also be studied for pancreatitis, light sensitivity and bone safety. All three drugs are given by mouth once daily. The usual starting dose is 100-300 mg for INVOKANA, 5-10 mg for FARXIGA, and 10-25 mg for JARDIANCE. The cost of treatment is about \$300 (WAC) for a month's supply of tablets.^{58,59,60,61,62} Do not confuse FARXIGA with the anti-depressant FETZIMA (levomilnacipran).¹

Two new once-weekly subcutaneously injected glucagon-like peptide-1 (GLP-1) receptor agonists were approved in 2014. This class of drugs works to lower blood sugar levels by increasing insulin, decreasing glucagon, slowing stomach emptying, and increasing the feeling of being full after eating. These should be used in addition to diet and exercise to treat type 2 diabetes, as is the case with other treatments for diabetes. **Albiglutide** (TANZEUM, approved 4/15/14) was evaluated in about 2,000 patients, while **dulaglutide** (TRULICITY, approved 9/18/14) was evaluated in about 3,000 patients. Both drugs' clinical trials showed improved glucose control by decreasing HbA1c levels alone and in combination with other drugs for diabetes. Neither of these new GLP-1 agonists should be used in patients with type 1 diabetes, gastrointestinal problems, or as a first-line treatment for type 2 diabetes. Prescribing information for both of these products includes a black box warning about an increased risk for thyroid tumors. Common side effects for this drug class include diarrhea, nausea, and injection site reactions. The recommended starting dose of albiglutide is 30 mg once weekly and can be increased to 50 mg. The starting dose of dulaglutide is 0.75 mg once weekly and may be increased to a maximum of 1.5 mg once weekly. Subcutaneous injections should be into the abdomen, thigh, or upper arm. Both drugs should be stored in the refrigerator in their original container. Dulaglutide comes in a liquid dosage form, while albiglutide must be reconstituted by twisting the cartridge pen to engage dilution of a powder. During use, dulaglutide can be stored at room temperature for up to 2 weeks, while albiglutide can be stored at room temperature for up to 4 weeks. Both

should be stored in their original containers to protect the drug from light. The FDA is requiring post-market clinical trials for both of these drugs. Albiglutide must be tested for cancer, cardiac, and pediatric safety, while dulaglutide must additionally be tested for maturation safety in animals and renal impairment safety in humans. The monthly cost (WAC) of albiglutide is about \$325, and about \$490 for dulaglutide.^{63,64,65} Because of safety concerns, the FDA has also required a Risk Evaluation and Mitigation Strategy (REMS) for each of these products. Both were approved with a communication plan that informs prescribers of the products' risks.⁶⁶

The first inhaled rapid-acting insulin product was approved in 2006, but was withdrawn from the market a year later, primarily due to inhaler size, cost, and difficulty of use. In 2014, another **inhaled human insulin** (AFREZZA, approved 6/27/14) was evaluated by the FDA, this one with a much smaller and easier to use breath-powered inhaler device. As with other insulin products, AFREZZA is a recombinant form of human insulin, but it is in a dry-powder rather than liquid form. It can be used in both type 1 and type 2 diabetes, but is approved in adults only. When used in type 1 diabetes, a long-acting insulin must also be used. It can be used in combination with other anti-diabetic drugs in type 2 diabetes. The product was evaluated in over 1,000 type 1 diabetics and almost 2,000 type 2 diabetics. In type 1 diabetics, AFREZZA HbA1c reduction was found to be clinically similar to that produced by insulin aspart (NOVOLOG). In type 2 diabetics, in combination with metformin or other oral antidiabetic drugs, AFREZZA reduced HbA1c better than those treated with placebo. Prescribing information includes a black box warning about the risk of bronchospasm, and for this reason it should not be used in patients with asthma or COPD. Smokers should not use the product, nor should those who stopped smoking less than six months ago. Common side effects include low blood sugar, cough, and throat irritation. The starting dose for patients new to insulin is 4 units by inhalation at the beginning of each meal. The dose is then adjusted clinically. The inhaler device is used for 15 days and then replaced. The FDA is requiring post-market clinical trials related to cancer, pharmacokinetics, and pediatric safety. The monthly cost (WAC) is about \$275.^{67,68} AFREZZA was approved with a REMS communication plan that informs prescribers of the product's risks.⁶⁶ See **Table 10** (page 16-17).

Table 10. New Drugs for Endocrinology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description, "Imprint" (Quantity)	Storage Conditions
Albiglutide (TANZEUM) ^a <i>Approved 4/15/14</i>	Lyophilized powder for subcutaneous injection	0173-0866-01 0173-0866-35 0173-0867-01 0173-0867-35	30 mg single-dose pen (1) 30 mg single-dose pens (4) 50 mg single-dose pen (1) 50 mg single-dose pens (4)	Before dispensing, store in refrigerator. Patients may store at room temperature for 4 weeks. Do not freeze. Use within 8 hours after reconstitution.
Alogliptin (NESINA) ^b <i>Approved 1/25/13</i>	Oral tablets	64764-625-30 64764-625-30 64764-125-30 64764-125-90 64764-125-50 64764-250-30 64764-250-90 64764-250-50	6.25 mg light pink oval tablet (30) 6.25 mg light pink oval tablet (90) >> marked "TAK ALG-6.25" 12.5 mg yellow oval tablet (30) 12.5 mg yellow oval tablet (90) 12.5 mg yellow oval tablet (500) >> marked "TAK ALG-12.5" 25 mg light red oval tablets (30) 25 mg light red oval tablets (90) 25 mg light red oval tablets (500) >> marked "TAK ALG-25"	Store at room temperature.
Alogliptin & metformin (KAZANO) ^c <i>Approved 1/25/13</i>	Oral tablets	64764-335-60 64764-335-80 64764-335-77 64764-337-60 64764-337-80 64764-337-77	12.5 mg alogliptin & 500 mg metformin pale yellow oblong tablets (60) 12.5 mg alogliptin & 500 mg metformin pale yellow oblong tablets (180) 12.5 mg alogliptin & 500 mg metformin pale yellow oblong tablets (500) >> marked "12.5/500" and "322M" 12.5 mg alogliptin & 1000 mg metformin pale yellow oblong tablets (60) 12.5 mg alogliptin & 1000 mg metformin pale yellow oblong tablets (180) 12.5 mg alogliptin & 1000 mg metformin pale yellow oblong tablets (500) >> marked "12.5/1000" and "322M"	Store at room temperature. Keep container tightly closed.
Alogliptin & pioglitazone (OSENI) ^d <i>Approved 1/25/13</i>	Oral tablets	64764-121-03 64764-121-04 64764-121-05 64764-123-03 64764-123-04 64764-123-05 64764-124-03 64764-124-04 64764-124-05 64764-251-03 64764-251-04 64764-251-05 64764-253-03 64764-253-04 64764-253-05 64764-254-03	12.5 mg alogliptin & 15 mg pioglitazone pale yellow oblong tablets (30) 12.5 mg alogliptin & 15 mg pioglitazone pale yellow oblong tablets (90) 12.5 mg alogliptin & 15 mg pioglitazone pale yellow oblong tablets (500) >> marked "A/P" and "12.5/15" 12.5 mg alogliptin & 30 mg pioglitazone pale peach round tablets (30) 12.5 mg alogliptin & 30 mg pioglitazone pale peach round tablets (90) 12.5 mg alogliptin & 30 mg pioglitazone pale peach round tablets (500) >> marked "A/P" and "12.5/30" 12.5 mg alogliptin & 45 mg pioglitazone pale red round tablets (30) 12.5 mg alogliptin & 45 mg pioglitazone pale red round tablets (90) 12.5 mg alogliptin & 45 mg pioglitazone pale red round tablets (500) >> marked "A/P" and "12.5/45" 25 mg alogliptin & 15 mg pioglitazone yellow round tablets (30) 25 mg alogliptin & 15 mg pioglitazone yellow round tablets (90) 25 mg alogliptin & 15 mg pioglitazone yellow round tablets (500) >> marked "A/P" and "25/15" 25 mg alogliptin & 30 mg pioglitazone peach round tablets (30) 25 mg alogliptin & 30 mg pioglitazone peach round tablets (90) 25 mg alogliptin & 30 mg pioglitazone peach round tablets (500) >> marked "A/P" and "25/30" 25 mg alogliptin & 45 mg pioglitazone red round tablets (30)	Store at room temperature. Keep container tightly closed. Protect from moisture. Protect from humidity.

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description, "Imprint" (Quantity)	Storage Conditions
		64764-254-04 64764-254-05	25 mg alogliptin & 45 mg pioglitazone red round tablets (90) 25 mg alogliptin & 45 mg pioglitazone red round tablets (500) >> marked "A/P" and "25/45"	
Canagliflozin INVOKANA ^e Approved 3/29/13	Oral tablets	50458-140-30 50458-140-90 50458-140-50 50458-140-10 50458-141-30 50458-141-90 50458-141-50 50458-141-10	100 mg yellow capsule-shaped tablets (30) 100 mg yellow capsule-shaped tablets (90) 100 mg yellow capsule-shaped tablets (500) 100 mg yellow capsule-shaped tablets (10x10) >> marked "CFZ" and "100" 300 mg white capsule shaped tablets (30) 300 mg white capsule shaped tablets (90) 300 mg white capsule shaped tablets (500) 300 mg white capsule shaped tablets (10x10) >> marked "CFZ" and "300"	Store at room temperature.
Dapagliflozin (FARXIGA) ^f Approved 1/8/14	Oral tablets	0310-6205-30 0310-6210-30	5 mg yellow round tablets (30) >> marked "5" and "1427" 10 mg yellow diamond-shaped tablets (30) >> marked "10" and "1428"	Store at room temperature.
Dulaglutide (TRULICITY) ^g Approved 9/18/14	Subcutaneous injection	0002-1433-80 0002-1434-80 0002-1431-80 0002-1432-80	0.75 mg / 0.5 mL single-dose pens (4) 1.5 mg / 0.5 mL single-dose pens (4) 0.75 mg / 0.5 mL single-dose syringes (4) 1.5 mg / 0.5 mL single-dose syringes (4)	Refrigerate. Patient may store at room temperature for 14 days. Do not freeze. Protect from light. Discard in puncture-resistant container.
Empagliflozin (JARDIANCE) ^h Approved 8/1/14	Oral tablets	0597-0152-30 0597-0152-90 0597-0152-37 0597-0153-30 0597-0153-90 0597-0153-37	10 mg pale yellow round tablets (30) 10 mg pale yellow round tablets (90) 10 mg pale yellow round tablets (3x10) >> marked "S 10" and company symbol 25 mg pale yellow oval tablets (30) 25 mg pale yellow oval tablets (90) 25 mg pale yellow oval tablets (3x10) >> marked "S 25" and company symbol	Store at room temperature.
Insulin human, inhaled (AFREZZA) ⁱ Approved 6/27/14	Inhalation powder	0024-5874-90 0024-5878-90 0024-5884-63 0024-5882-36 0024-5880-18 0024-5890-90 0024-5893-36 0024-5894-63 0024-5895-33	4 unit cartridges (90), inhalers (2) 8 unit cartridges (90), inhalers (2) 4 unit cartridges (60), 8 unit cartridges (30), inhalers (2) 4 units cartridges (30), 8 unit cartridges (60), inhalers (2) 4 unit cartridges (90), 8 unit cartridges (90), inhalers (2) 12 unit cartridges (90), inhalers (2) 8 unit cartridges (30), 12 unit cartridges (60), inhalers (2) 8 unit cartridges (60), 12 unit cartridges (30), inhalers (2) 4 unit cartridges (30), 8 unit cartridges (30), 12 unit cartridges (30), inhalers (2)	Refrigerate. If at room temperature, sealed strips must be used with 10 days. If at room temperature, opened strips must be used within 3 days. Cartridges should be at room temperature for 10 minutes prior to use. Inhalers may be refrigerated but should be brought to room tem- perature prior to use.

^a TANZEUM (albiglutide) [package insert]. GlaxoSmithKline LLC; May 2015.

^b NESINA (alogliptin) [package insert]. Takeda Pharmaceuticals America, Inc.; January 2013.

^c KAZANO (alogliptin and metformin) [package insert]. Takeda Pharmaceuticals America, Inc.; January 2013.

^d OSENI (alogliptin and pioglitazone) [package insert]. Takeda Pharmaceuticals America, Inc.; January 2013.

^e INVOKANA (canagliflozin) [package insert]. Janssen Pharmaceuticals, Inc.; March 2015

^f FARXIGA (dapagliflozin) [package insert]. AstraZeneca Pharmaceuticals LP; March 2015

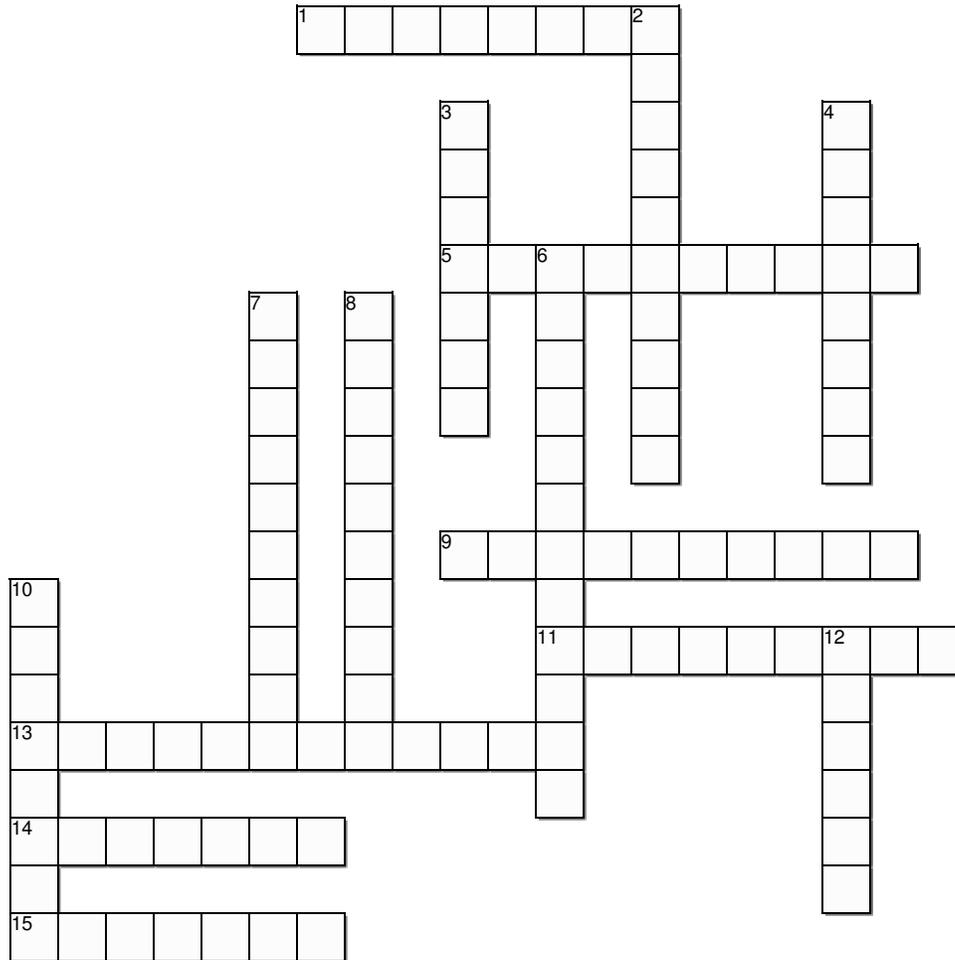
^g TRULICITY (dulaglutide) [package insert]. Eli Lilly and Company; March 2015.

^h JARDIANCE (empagliflozin) [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc.; August 2014.

ⁱ AFREZZA (insulin human, inhaled) [package insert]. Sanofi-Aventis U.S. LLC; April 2015

New Drugs Crossword Puzzle B

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

1. BELSOMRA indication.
5. Route of administration for ORALAIR, RAGWITEK, and GRASTEK.
9. The “gliptin” component of KAZANO and OSENI.
11. Peginterferon beta-1a (PLEGRIDY) is a _____ form of interferon beta-1a.
13. Route of administration for PLEGRIDY.
14. GLP-1 receptor agonists decrease blood sugar by increasing _____.
15. SGLT2 inhibitors decrease blood sugar by increasing kidney excretion of _____.

Down

2. The generic name for OTEZLA.
3. Levomilnacipran (FETZIMA) capsules should not be _____.
4. The generic name for TECFIDERA is dimethyl _____.
6. AFREZZA brand human insulin has a black box warning for _____.
7. The generic name for BELSOMRA.
8. Route of administration of AFREZZA brand human insulin.
10. _____ decreases when TECFIDERA is taken with food.
12. Vortioxetine (BRINTELLIX) dosage form.

Answers on page 54.

Hematology (Blood Disorders)

Iron Deficiency Anemia

When iron stores drop too low to support red blood cell production, anemia occurs. Symptoms include fatigue, decreased abilities, leg cramps, slowed speech, decreased resistance to infection, and sometimes compulsive eating of ice. The goals of treatment include correcting the underlying problem and replacing iron stores. Treatment may include oral iron, parenteral iron, or packed red blood cells. The route of administration for iron replacement is based on the severity of the deficiency, vein access, prior response, adherence to treatment, and cost.⁶⁹

Ferric carboxymaltose (INJECTAFER, approved 7/25/13) is a colloidal iron complex for the treatment of adults with iron deficiency anemia who can't take or have not had a good response to oral iron. It is the sixth parenteral iron product on the market. Clinical trials of ferric carboxymaltose showed a significant improvement in hemoglobin as compared with baseline iron sucrose, and oral iron. Hypersensitivity reactions are possible, with anaphylaxis occurring in two patients during clinical trials. However, the rate of anaphylaxis with ferric carboxymaltose is lower than that seen with iron dextran (DEXFERRUM, INFED). Adverse drug reactions include nausea, high blood pressure, flushing, low blood phosphate, and dizziness. The treatment is given in two doses, 750 mg intravenously, followed by another 750 mg dose a week later. Unlike iron dextran, no test dose is needed for ferric carboxymaltose. It is administered either by intravenous infusion over 15 minutes in 250 milliliters normal saline, or by undiluted slow IV push injection given no faster than 100 mg per minute. Patients should be monitored for 30 minutes after each administration. If an IV containing ferric carboxymaltose extravasates, or leaks out of the vein, a long-lasting brown discoloration will occur. The undiluted 750 mg iron/15 mL single-dose vial is stored at room temperature. Once diluted to concentrations of 2 mg to 4 mg iron per mL, it has a 72 hour beyond use date at room temperature. The cost is \$1,500 (WAC) for the 2-dose regimen.⁷⁰

Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia (ALL) is a malignant (cancerous) bone marrow disease in which precursor cells increase significantly and replace normal cells. This is caused by abnormal gene expression. It is the most com-

mon cancer in American children. It is less common in adults. About 15% of patients have a chromosomal translocation known as Philadelphia chromosome. According to the National Cancer Institute, 6,000 people will be diagnosed and 1,440 will die of ALL in 2014. Since only 20-40% of adult patients are cured with current treatment regimens, most are placed in clinical trials for new regimen evaluation.⁷¹ **Blinatumomab** (BLINCYTO, approved 12/3/14) is a bi-specific T-cell engager (BiTE®), which means that it includes the binding sites of two different antibodies, bringing the T-cell to the affected B-cell by binding the T-cell's CD3 receptor to ALL B-cell's CD19 receptor, thus helping the T-cell to find normal and cancerous B-cell and destroy them. Blinatumomab is produced in Chinese hamster ovary cells and indicated for Philadelphia chromosome-negative ALL. It received accelerated approval by the FDA because after two cycles of blinatumomab in a clinical trial, one-third of patients that previously failed on other therapy reached complete remission for an average of 6.7 months. Prescribing information includes a black box warning for Cytokine Release Syndrome and neurological toxicity. There are additional warnings about susceptibility to infection, impaired driving, preparation errors, administration errors, increased liver enzymes, and tumor lysis syndrome caused by the release of killed cancer cell contents. Common adverse effects include fever, headache, nausea, shakiness, seizures, rash, edema, constipation, low potassium levels, and lowered white blood cell counts. The drug is available as a 35 mcg lyophilized powder in a single-dose vial and it is packaged with a 10 mL single-use vial of IV solution stabilizer, which should NOT be used to reconstitute the drug. Blinatumomab is reconstituted with preservative-free sterile water for injection. The reconstituted drug solution has a beyond-use dating of 4 hours at room temperature and 24 hours in the refrigerator. In a separate step, the stabilizer is added to normal saline. The reconstituted drug is then added to the stabilized normal saline for a beyond-use date of 48 hours at room temperature and 8 days refrigerated. The diluted drug/stabilizer/saline bag is used to perform very specific dilutions for 24-hour and 48-hour bags. Only polyolefin, non-DEHP, or EVA bags may be used. Administration sets must be attached to the infusion bags during the sterile compounding process. The drug is administered as a continuous IV infusion through a programmable electronic ambulatory infusion pump. An elastomeric infusion pump may NOT be used for this drug's complex administration protocol. The drug is administered at 9 mcg per day for days 1 through 7 in the hospital, and then 28 mcg per day for

days 8 through 28. Days 8 and 9 are also administered within a hospital setting. The patient is given 2 weeks off, and then given 28 mcg per day for days 1 through 28, followed by cycles of 2 weeks off and 28-day drug cycles for a total of up to five cycles. Dexamethasone is used as a pre-medication one hour prior to each treatment cycle. Dose adjustment is required for Cytokine Release Syndrome or neurotoxicity. The cost of a 6-week treatment is \$60,400 (WAC).^{72,73} BLINCYTO was approved with a REMS communication plan that informs prescribers of the product's risks.⁶⁶

Chronic Lymphocytic Leukemia

About 17,000 new cases of chronic lymphocytic leukemia (CLL) occur each year. CLL is a bone marrow cancer in which incompetent lymphocytes gradually accumulate. The median age of diagnosis is 72 years old. Some patients die within two to three years of diagnosis, while most live five to ten years. The goals of treatment include complete response, minimized disease, improved response duration, and progression-free survival. Early stage CLL is not treated, but as soon as symptoms (recurring infections, loss of appetite, enlarged lymph nodes, bruising, tiredness, night sweats) start, combination chemotherapy and biologic agents are initiated.⁷⁴ Three drugs were approved in 2013 and 2014 for the treatment of CLL: **obinutuzumab** (GAZYVA, approved 11/1/13), **ibrutinib** (IMBRUVICA, approved 11/13/13), and **idelalisib** (ZYDELIG, approved 7/23/14).

Obinutuzumab is an anti-CD20 monoclonal antibody used in combination with chlorambucil (LEUKERAN) in patients with previously untreated CLL. It is the third anti-CD20 antibody approved for CLL. This class of antibodies binds to the CD20 antigen on B-cells and causes them to break apart. Clinical trials showed a significantly improved progression-free survival of almost 27 months with obinutuzumab and chlorambucil over chlorambucil alone (11 months) or rituximab (RITUXAN) with chlorambucil (16 months). Prescribing information includes a black box warning for hepatitis B reactivation and progressive multifocal leukoencephalopathy (PML). Adverse effects include risk of infection, infusion-related reactions, tumor lysis syndrome, decreased white blood cells, decreased platelets, decreased red blood cells, muscle pain, bone pain, and fever. The first two doses are prepared simultaneously by diluting in normal saline only in polyvinyl chloride (PVC) or polyolefin bags. Obinutuzumab should not be diluted in other solutions such as dextrose 5% and it should not be shaken. The dose on day

1 is 100 mg administered at 25 mg/hour as an intravenous infusion. The dose on day two is 900 mg infused initially at 50 mg/hour. The rate can be increased in 30 minute intervals by 50 mg/hour up to a maximum of 400 mg/hour. On day 8, 15, and every 28 days for 5 more cycles, 1000 mg is administered initially at 200 mg/hour, increased in 30 minute intervals by 100 mg/hour up to a maximum of 400 mg/hour. Patients may be premedicated initially with a glucocorticoid, acetaminophen and an antihistamine. Subsequent cycles can include premedication with just acetaminophen if an infusion reaction has not been previously experienced. The cost of one cycle of treatment is \$5,200 (WAC).^{75,76,77}

Idelalisib (ZYDELIG) and **ibrutinib** (IMBRUVICA) are both oral kinase inhibitors. This class of drugs prevents the production of cancerous B-cells and increases their death rate. Idelalisib is used in combination with rituximab (RITUXAN) for relapsed CLL. In clinical trials, patients received idelalisib and rituximab or placebo and rituximab. Patients treated with idelalisib and rituximab were found to have a progression-free survival of almost 11 months, while those with rituximab alone was less than 6 months. Prescribing information includes a black box warning for liver toxicity, colitis, lung inflammation, and intestinal perforation. Side effects include diarrhea, fever, tiredness, nausea, cough, lung infection, abdominal pain, chills, rash, decreased white blood cells, increased triglycerides, high blood sugar, bleeding, and increased liver enzymes. The dose is 150 mg twice daily with or without rituximab until progression or intolerable toxicity. Tablets should not be chewed or crushed. The cost of a month's treatment with idelalisib is approximately \$8,000 (WAC).^{78,79} Idelalisib was approved with a REMS communication plan that informs prescribers of the product's risks.⁶⁶

Ibrutinib (IMBRUVICA) was additionally approved 2/12/14 as a second-line treatment for CLL in patients who have had at least one previous treatment and on 2/28/14 for CLL with a 17p deletion. This type of CLL has had very poor response to treatment. Clinical trials showed that 58% of patients showed an overall response rate, meaning that their cancer shrank. The most common side effects are decreased platelets, diarrhea, bruising, decreased white blood cells, decreased red blood cells, upper respiratory tract infection, fatigue, muscle pain, bone and joint pain, rash, fever, constipation, edema, nausea, mouth sores, and dizziness. Be aware that there are significant drug interactions. The dose is 420 mg (three 140 mg capsules) once daily with a glass of water. The tablets should not be crushed or chewed. The cost of one month's treatment for CLL is about \$8,200 (WAC).^{80,81}

Mantle Cell Lymphoma

Mantle cell lymphoma (MCL) is a rare and aggressive non-Hodgkin lymphoma that has spread to the lymph nodes, bone marrow, and organs by the time it is diagnosed. While **ibrutinib** (IMBRUVICA) is the third drug for MCL, it was its first indication. In a clinical trial for MCL, 66% of patients showed an overall response rate, meaning that the cancer had either shrunk or disappeared. The dose in MCL is 560 mg (four 140 mg capsules) once daily with a glass of water. Please see CLL discussion above for ibrutinib side effects.^{82,83} Based on the cost of treatment for CLL, one month's treatment for MCL costs about \$11,000 (WAC).

Multiple Myeloma

Multiple myeloma (MM) is a blood cancer that affects plasma cells that form antibodies, leading to impaired immunity, infection, high blood viscosity, and kidney failure. MM accounts for 10% of all blood cancers. The American Cancer Society estimates that almost 27,000 new MM cases will be diagnosed in 2015 and about 11,250 will die from the disease. Survival ranges from 1 to 10 years, and the 5-year survival rate is 47%. Survival is better in younger than older people. **Pomalidomide** (POMALYST, approved 2/28/13) is similar to thalidomide and has a black box warning for blood clots and teratogenicity (birth defects). It works by increasing MM cell death. Clinical trials showed better progression-free survival in patients treated with pomalidomide and dexamethasone than in patients treated with pomalidomide alone. Adverse effects include deep vein thrombosis, pulmonary embolism, tumor lysis syndrome, dizziness, confusion, and nerve pain. Side effects include weakness, tiredness, fever, upper respiratory tract infection, constipation, diarrhea, nausea, and back pain. Because it can cause fetal damage, women must have two negative pregnancy tests before they are started on pomalidomide, and should use two types of contraception during treatment and a month after stopping the drug. Men treated with pomalidomide should use a condom during medication treatment and for one month after. Because of its danger during pregnancy, pomalidomide has a REMS program that requires assurance for safe use and an implementation system.⁶⁶ For this reason it is only available through a restricted drug distribution program. The usual starting dose is 4 mg once daily by mouth for the initial 21 days of a 28-day cycle. This cycle is continued until the disease progresses or unacceptable toxicity is experienced. Phar-

macies can dispense only a 4-week (28 day) supply with no refills. Patients need to be counseled by the pharmacist. The capsules should be taken whole, and should not be broken, opened, or chewed. The dose may be adjusted if certain adverse effects occur or if taken with drugs that interact by increasing pomalidomide levels. The cost of one 28-day treatment cycle is about \$11,500 (WAC).^{84,85,86}

Peripheral T-cell Lymphoma

Peripheral T-cell lymphoma (PTCL) is a rare and aggressive blood cancer. Of the 70,800 cases and 19,000 deaths from non-Hodgkin lymphoma estimated for 2014, approximately 10-15% will be due to PTCL. Treatment includes combination chemotherapy and blood cell transplant. **Belinostat** (BELEODAQ, accelerated approval 7/3/14) is indicated for relapsed and refractory PTCL. It is a histone deacetylase inhibitor that causes death preferentially in cancer cells. A complete or partial response was seen in 26% of patients in clinical trials and the median duration of response was a little over 8 months. Additional trials are needed to see if the drug improves overall survival. Adverse effects include decreased platelets, decreased white blood cells, anemia, infection, liver toxicity, tumor lysis syndrome, gastrointestinal toxicity, and fetal toxicity. Side effects include nausea, fatigue, fever, and vomiting. There are significant drug interactions. Chemotherapy precautions are required for handling, preparation, and administration. The drug is reconstituted with sterile water for a beyond-use date of 12 hours at room temperature. The reconstituted solution is further diluted in 250 mL normal saline. The diluted product has a beyond-use date of 36 hours at room temperature, including the infusion time. The dose of 1,000 mg per meter squared is given intravenously over 30-45 minutes through a 0.22 micron in-line filter. The dose is administered daily on days 1 through 5 of a 21-day cycle until disease progression or unacceptable toxicity. The dose is modified for certain adverse effects and discontinued after two dosage adjustments have been attempted. The cost for six month's treatment is about \$240,000 (WAC).^{87,88,89} See **Table 11** (page 22).

Oncology (Cancer)

Skin Cancer

Melanoma is a cancer of skin cells known as melanocytes. Its incidence is increasing by 6% annually. Risk factors

Table 11. New Drugs for Hematology (excluding Orphan Drugs)

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Belinostat (BELEODAQ) ^a <i>Approved 7/3/14</i>	Lyophilized powder for injection	68152-108-09	500 mg single-use vial	Store at room temperature. Chemotherapy precautions.
Blinatumomab (BLINCYTO) ^b <i>Approved 12/3/14</i>	Lyophilized powder for injection	55513-160-01	35 mcg single-use vial (1) 10 mL IV solution stabilizer (1)	Refrigerated. Do not freeze. Protect from light.
Ferric carboxymaltose (INJECTAFER) ^c <i>Approved 7/25/13</i>	Injection	0517-0650-01 0517-0650-02	75 mg iron / 15 mL single-use vial (1) 75 mg iron / 15 mL single-use vials (2)	Store at room temperature. Do not freeze.
Ibrutinib (IMBRUVICA) ^d <i>Approved 11/13/13</i>	Oral capsule	57962-140-09 57962-140-12	140 mg white capsules (90) 140 mg white capsules (120) >> marked “ibr 140 mg” in black	Store at Room Temperature.
Idelalisib (ZYDELIG) ^e <i>Approved 7/23/14</i>	Oral tablet	61958-1701-1 61958-1702-1	100 mg orange oval tablet (60) >> marked “100” and “GSI” 150 mg pink oval tablet (60) >> marked “150” and “GSI”	Store at room temperature Dispense in original container.
Obinutuzumab (GAZYVA) ^f <i>Approved 11/1/13</i>	Injection for intravenous infusion	50242-070-01	100 mg / 40 mL single-use vial (1)	Refrigerate. Protect from light. Do not freeze. Do not shake.
Pomalidomide (POMALYST) ^g <i>Approved 2/8/13</i>	Oral capsules	59572-501-21 59572-501-00 59572-502-21 59572-502-00 59572-503-21 59572-503-00 59572-504-21 59572-504-00	1 mg dark blue and yellow capsule (21) 1 mg dark blue and yellow capsule (100) >> marked “POML” and “1 mg” 2 mg dark blue and orange capsule (21) 2 mg dark blue and orange capsule (100) >> marked “POML” and “2 mg” 3 mg dark blue and green capsule (21) 3 mg dark blue and green capsule (100) >> marked “POML” and “3 mg” 4 mg dark blue and blue capsule (21) 4 mg dark blue and blue capsule (100) >> marked “POML” and “4 mg”	Store at room temperature. Chemotherapy precautions.
Siltuximab (SYLVANT) ^h <i>Approved 4/23/14</i>	Injection for intravenous infusion	57894-420-01 57894-421-01	100 mg single-use vial (1) 400 mg single-use vial (1)	Refrigerate. Protect from light. Preservative free.

^a BELEODAQ (belinostat) [package insert]. Spectrum Pharmaceuticals, Inc.; July 2014.

^b BLINCYTO (blinatumomab) [package insert]. Amgen, Inc.; December 2014.

^c INJECTAFER (ferric carboxymaltose) [package insert]. American Regent, Inc.; July 2013

^d IMBRUVICA (ibrutinib) [package insert]. Pharmacyclics, Inc.; January 2015.

^e ZYDELIG (idelalisib) [package insert]. Gilead Sciences, Inc.; July 2014.

^f GAZYVA (obinutuzumab) [package insert]. Genentech, Inc.; December 2014.

^g POMALYST (pomalidomide) [package insert]. Celgene Corporation; April 2015.

^h SYLVANT (siltuximab) [package insert]. Janssen Biotech, Inc.; June 2014.

include a family history of melanoma, fair complexion, weakened immune system, and sun exposure. Melanoma presents itself as a lop-sided lesion with an irregular border, varied color, elevated surface and a diameter greater than 6 millimeters. Diagnosis is made by doing a full thickness biopsy. In early melanoma, the best treatment is surgical removal of the lesion. If not removed, the lesion may become metastatic, with the cancer spreading to other sites through the lymphatic system. At this stage, it requires systemic (internal) anti-cancer treatment. Metastatic melanoma is the leading cause of death from skin disease.^{90,91}

Two oral kinase inhibitors were approved for metastatic melanoma: **dabrafenib** (TAFINLAR, approved 5/29/13) and **trametinib** (MEKINIST, approved 5/29/13). These drugs work by causing death in melanoma cells and are used individually or in combination. While they work on the same molecular pathway, they seem to work at different sites. Each was approved with a diagnostic kit that tests whether the patient's melanoma cells would be susceptible to the treatment. Dabrafenib was compared to dacarbazine (DTIC) in a clinical trial. Patients treated with dabrafenib showed a 2 month delay in tumor growth. Side effects included increased risk of other skin cancer, fever, low blood pressure, shaking chills, dehydration, increased blood sugar, kidney failure, skin thickening, headache, joint pain, and hair loss. Trametinib was compared with chemotherapy in another clinical trial. Patients treated with trametinib showed a 3 month delay in tumor growth. In patients who received previous kinase inhibitor treatment, trametinib did not show a benefit. Side effects included heart failure, lung inflammation, skin infections, vision loss, rash, diarrhea, edema, and acne-like breakouts. About six months after their individual approvals, dabrafenib and trametinib were approved to be used together in the treatment of late-stage melanoma. The combination showed that 76% of patients had cancer shrinkage or disappearance that lasted almost 11 months. When treated with dabrafenib alone, 54% showed the same response for a little over 5 months. It is unknown yet whether this combination of drugs improves survival in late-stage melanoma. The side effect profile of these two drugs is similar to that seen with each individual drug, except that the incidence of other skin cancers seen with dabrafenib was decreased when used in combination with trametinib. Both drugs can cause fetal harm and increase the risk of infertility. Dabrafenib has multiple drug interactions, while trametinib does not. The dosing for dabrafenib is 150 mg (two 75 mg capsules)

orally every 12 hours; and the dosing for trametinib is 2 mg orally once daily. Both should be taken 1 hour before or 2 hours after a meal. Treatment is continued until disease progression or intolerable side effects occur. The cost of one month's treatment of dabrafenib is \$7,600 (WAC), while the cost of one month's treatment with trametinib is \$8,700.^{92,93,94}

Two monoclonal antibodies that block the human programmed death receptor-1 were approved in 2014 for use in late-stage melanoma: **pembrolizumab** (KEYTRUDA, approved 9/4/14) and **nivolumab** (OPDIVO, approved 12/22/14). In a clinical trial, 24% of tumors shrank in pembrolizumab-treated patients and about 60% experienced a 1-year survival. Serious adverse effects include many immune-related effects and this drug is toxic to the fetus. Side effects include fatigue, cough, nausea, itching, rash, decreased appetite, constipation, joint pain, and diarrhea. When the lyophilized powder is reconstituted with sterile water, the solution has a beyond-use date of 6 hours at room temperature and 24 hours refrigerated. Do not shake the vial. The dose is 2 mg/kg given as an intravenous infusion through a 0.2-5 micron in-line filter over 30 minutes every 3 weeks until disease progression or unacceptable toxicity. The dose is held, restarted, and discontinued for certain adverse effects. The cost of 6 month's treatment is \$58,000 (WAC).^{95,96,97} In a clinical trial, 32% of patients treated with nivolumab (OPDIVO) showed tumor shrinkage, and the effect lasted for more than six months. Serious adverse effects include immune-related reactions, fetal toxicity, rash, itching, cough, upper respiratory tract infection, and edema. The drug is available in liquid form and is diluted with normal saline or dextrose 5% in water. The beyond-use date after dilution is 4 hours at room temperature and 24 hours refrigerated. The 3 mg/kg dose is given as an intravenous infusion through a 0.2 to 1.2 micron in-line filter over 60 minutes every 2 weeks until disease progression or unacceptable toxicity. The dose is held, resumed, and discontinued for certain adverse effects.^{98,99}

Lung Cancer

Non-small cell lung cancers (NSCLC) account for about 85% of all lung cancers. The major causes of lung cancer include smoking and exposure to other environmental carcinogens. About 90% of all lung cancer is caused by smoking. The American Cancer Society estimated that 219,000 cases of lung cancer would be diagnosed in 2009. Unfortunately, lung cancer is deadly. In 2009, it account-

ed for 28% of all cancer deaths. Treatment includes surgery, chemotherapy, and radiation. Additionally, because most lung cancers cannot be cured, palliative (comfort measure) care becomes very important.¹⁰⁰

Two tyrosine kinase inhibitors were approved for use in NSCLC in 2013 and 2014, one for cancer cells that express EGFR mutations and the other whose cells are ALK-positive. **Afatinib** (GILOTRIF, approved 7/12/13) is a tyrosine kinase inhibitor that was approved with a companion diagnostic kit that identifies whether the patient's cancer cells express EGFR mutations. In comparison with patients who received the anticancer drugs, pemetrexed and cisplatin, patients who received afatinib had a 4 month delay in tumor growth. Survival did not differ significantly. Serious adverse effects include severe diarrhea, kidney failure, severe dehydration, severe rash, lung inflammation, liver toxicity, acne-like skin breakouts, dry skin, itching, decreased appetite, decreased weight, bladder inflammation, nose bleeds, runny nose, fever, eye inflammation and low blood potassium. The recommended dose is 40 mg by mouth once daily taken 1 hour before or 2 hours after a meal.^{101,102} **Ceritinib** (ZYKADIA, approved 4/29/14) is an ALK kinase inhibitor indicated for patients with ALK-positive NSCLC that were previously given crizotinib (XALKORI). In a clinical trial, 50% of patients showed cancer shrinkage for an average of 7 months. Serious adverse effects include increased liver enzymes, increased pancreatic enzymes, increased blood glucose, diarrhea, nausea, vomiting, and abdominal pain. There are significant drug interactions. The drug may cause fetal harm. The dose is 750 mg (five 150 mg capsules) orally once daily on an empty stomach.^{103,104}

Gastric (Stomach) Cancer

Gastric cancer is the fifteenth most common type of cancer in the United States. At one time it was the second most common. Its decreased incidence over the past 50 years is due to refrigeration, increased consumption of fruits and vegetables, and treatment of *H. pylori* infection. In 2015, it is estimated that there will be 24,500 new cases and 10,500 deaths due to gastric cancer. Unfortunately, symptoms do not appear until the disease is advanced, and it mostly affects older adults. Symptoms include indigestion, nausea, vomiting, difficulty swallowing, fullness after eating, no appetite, anemia, throwing up blood, weight loss, and enlarged lymph nodes. Treatment includes surgery, chemotherapy, and palliative care.¹⁰⁵

Ramucirumab (CYRAMZA, approved 4/21/14) is a monoclonal antibody angiogenesis inhibitor that blocks the blood

supply to tumors. It should be used in patients whose cancer has spread after treatment or whose cancer cannot be treated with surgery. Patients treated with ramucirumab lived about 1.5 months longer than those on placebo. In another trial, survival improved by 2.2 months when administered with paclitaxel (TAXOL). Adverse effects include diarrhea, high blood pressure, low white blood cells, tiredness, mouth sores, and nosebleeds. Prescribing information includes a black box warning for hemorrhage. There is also an increased risk of thrombosis, gastrointestinal perforation and decreased wound healing with this treatment. The drug is prepared by diluting the vials with normal saline to a final volume of 250 mL. It should not be shaken and stability is 4 hours at room temperature or 24 hours refrigerated. Ramucirumab should NOT be diluted in dextrose 5% in water. The dose in gastric cancer is 8 mg/kg intravenously over one hour by infusion pump every two weeks, with or without paclitaxel, until disease progression or unacceptable adverse effects. If given with paclitaxel, ramucirumab should be administered first. Patients should be premedicated with an antihistamine. Those who experience infusion related reactions should be premedicated with a corticosteroid and acetaminophen. The dose is adjusted, restarted, or discontinued with adverse effects. The cost of one vial of ramucirumab is \$5,100 (WAC).^{106,107} The drug is also approved for advanced NSCLC with or without docetaxel (TAXOTERE). The dose in NSCLC is 10 mg/kg intravenously over one hour by infusion pump with or without docetaxel on day 1 of a 21-day cycle until disease progression or unacceptable adverse effects. If administered with docetaxel, ramucirumab is administered first.^{108,109}

Breast Cancer

In the United States, breast cancer is the second leading cause of cancer-related death in women, after lung cancer. In 2015, 230,000 new cases are anticipated, with 40,000 estimated deaths. Although diagnosis of breast cancer has been increasing, deaths have been decreasing. This trend might be attributed to earlier detection and decreases in the use of hormone replacement therapy. Treatment options for late stage breast cancer resistant to other therapies include capecitabine (XELODA) and/or ixabepilone (IXEMPRA).¹¹⁰ HER2, a growth factor receptor on breast cancer cells, is overexpressed in about 20% of advanced breast cancers. Before trastuzumab (HERCEPTIN), HER2 positive breast cancer had a worse prognosis than HER2 negative breast cancer. Today, two-thirds of HER2-positive breast cancers treated with trastuzumab develop resistance.¹¹¹

Ado-trastuzumab emtansine (KADCYLA, approved 2/22/13) is a novel monoclonal antibody that has attached the anti-cancer drug DM1 to the trastuzumab molecule. The trastuzumab portion of the molecule searches out HER2 receptors and delivers DM1 directly into the breast cancer cell, which stops the cell cycle and causes death of the breast cancer cell. This is truly a “targeted” therapy! Ado-trastuzumab emtansine was compared to lapatinib (TYKERB) with capecitabine (XELODA) in clinical trial. Treatment with ado-trastuzumab emtansine resulted in a nearly 6 month longer survival than the oral combination. Ado-trastuzumab was approved for single-drug treatment of HER2 positive breast cancer that previously failed trastuzumab and taxane treatment. Prescribing information includes a black box warning against liver, heart, and fetal toxicity. Adverse effects include lung toxicity, infusion related reactions, hypersensitivity, nerve toxicity, low platelets, fatigue, nausea, muscle pain, bone pain, increased liver enzymes and constipation. It interacts with drugs that inhibit liver metabolism. Chemotherapy precautions are required for the handling, admixture, and preparation of this product. The drug is reconstituted with sterile water for injection and further diluted in 250 mL normal saline. Dextrose 5% in water should NOT be used to dilute ado-trastuzumab. Reconstituted vials can be stored in the refrigerator up to 24 hours. The dose is 3.6 mg/kg intravenously every three weeks until disease progression or intolerable toxicity. The first dose is administered over 90 minutes, if tolerated, subsequent doses can be given over 30 minutes. A 0.2 or 0.22 micron in-line polyethersulfone (PES) filter is used during administration and the patient should be observed for 30 minutes following each infusion. The cost per treatment cycle is \$7,200 (WAC).^{112,113,114} Do not confuse ado-trastuzumab emtansine (KADCYLA) with trastuzumab (HERCEPTIN). The prefix “ado” was added to distinguish between the two similar drugs.¹

Ovarian Cancer

Most cases of ovarian cancer are diagnosed in a later stage because symptoms are minimal during the early stages of the disease. Survival is proportional to the stage at diagnosis - the earlier the stage, the better the diagnosis. Unfortunately, the overall prognosis for ovarian cancer is poor. Treatment includes surgery and chemotherapy. It is estimated that about 21,000 new cases will be diagnosed and 14,000 women will die from ovarian cancer in 2015.¹¹⁵

Olaparib (LYNPARZA, approved 12/19/14) is a poly ADP-ribose polymerase (PARP) inhibitor indicated in advanced ovarian cancer that has a defective BRCA gene. It blocks enzymes that mend damaged DNA in the cancer cell. The drug was approved with a companion genetic test. About 15% of ovarian cancer has the BRCA mutation. Clinical trials with olaparib in women with the BRCA mutation showed that one-third of patients had a response for almost 8 months. Serious adverse effects include bone marrow suppression, leukemia, lung inflammation, decreased red blood cells, decreased white blood cells, increased serum creatinine, nausea, tiredness, vomiting, diarrhea, altered taste, indigestion, headache, diminished appetite, cold-like symptoms, cough, joint pain, muscle pain, bone pain, back pain, rash, and abdominal pain. The dose is 400 mg (eight 50 mg capsules) twice daily by mouth until disease progression or toxicity. Capsules should be swallowed whole. The dose may be interrupted or decreased for certain adverse reactions. Be aware that there are significant drug interactions.^{116,117} See **Table 12** (page 26).

Infectious Diseases

Acute Bacterial Skin and Skin Structure Infections

Acute bacterial skin and skin structure infections (ABSSSI) include cellulitis, wound infection, and cutaneous abscesses. In many parts of the United States, ABSSSIs are primarily caused by the microorganism, methicillin-resistant *Staphylococcus aureus* (MRSA). It should be noted that community-acquired MRSA infections are more virulent (highly infective) than those acquired in the hospital. Cellulitis is a relatively common localized condition. Death from it is rare. The goal of treatment is to eliminate the infection and prevent complications. Treatment options include oral antibiotics for mild localized infections and intravenous antibiotics for severe infections.¹¹⁸ Three new antibiotics were approved in 2014 to treat ABSSSI: **dalbavancin** (DALVANCE, approved 5/23/14), **tedizolid** (SIVEXTRO, approved 6/20/14), and **oritavancin** (ORBACTIV, approved 8/6/14).

Dalbavancin (DALVANCE) and **oritavancin** (ORBACTIV) are glycopeptides, in the same drug category as vancomycin and telavancin (VIBATIV). Glycopeptides inhibit microbe cell wall synthesis and are considered to be bactericidal (kill the bacteria). Clinical trials found dalbavancin to be equivalent to vancomycin followed by oral linezolid

Table 12. New Drugs for Oncology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Ado-trastuzumab emtansine (KADCYLA) ^a <i>Approved 2/22/13</i>	Lyophilized powder for intravenous infusion	50242-088-01 50242-087-01	100 mg single-use vial 160 mg single-use vial	Refrigerate. Do not freeze. Do not shake.
Afatinib dimaleate (GILOTRIF) ^b <i>Approved 7/12/13</i>	Oral tablets	0597-0141-30 0597-0137-30 0597-0138-30	20 mg with round tablets (30) >> marked “T20” and company symbol 30 mg dark blue round tablets (30) >> marked “T30” and company symbol 40 mg light blue round tablets (30) >> marked “T40” and company symbol	Store at room temperature. Protect from light. Protect from humidity. Dispense in original container.
Ceritinib (ZYKADIA) ^c <i>Approved 4/29/13</i>	Oral capsules	0078-0640-70	150 mg blue and white capsules (70) >> marked “LDK 150MG” and “NVR”	Store at room temperature.
Dabrafenib (TAFINLAR) ^d <i>Approved 5/29/13</i>	Oral capsules	0173-0846-08 0173-0847-08	50 mg dark red capsule (120) >> marked “GS TEW” and “50 mg” 75 mg dark pink capsule (120) >> marked “GS LHF” and “75 mg”	Store at room temperature.
Nivolumab (OPDIVO) ^e <i>Approved 12/22/14</i>	Injection	0003-3772-11 0003-3774-12	40 mg / 4 mL single-use vial (1) 100 mg / 10 mL single-use vial (1)	Refrigerate Protect from light. Do not freeze or shake.
Olaparib (LYNPARZA) ^f <i>Approved 12/19/14</i>	Oral capsules	0310-0657-58	50 mg white capsule (112) >> marked “OLAPARIB 50 mg” and logo	Store at room temperature.
Pembrolizumab (KEYTRUDA) ^g <i>Approved 9/4/14</i>	Lyophilized powder for injection solution	0006-3029-02 0006-3026-02	50 mg single-use vial (1) 100 mg/4 mL single-use vial	Refrigerate. Refrigerate.
Ramucirumab (CYRAMZA) ^h <i>Approved 4/21/14</i>	Injection	0002-7669-01 0002-7678-01	100 mg / 10 mL single-dose vial (1) 500 mg / 50 mL single-dose vial (1)	Refrigerate. Protect from light. Do not freeze or shake.
Trametinib (MEKINIST) ⁱ <i>Approved 5/29/13</i>	Oral tablets	0173-0849-13 0173-0858-13 0173-0848-13	0.5 mg yellow oval tablets (30) >> marked “GS” and “TFC” 1 mg white round tablets (30) >> marked “GS” and “LHE” 2 mg pink round tablets (30) >> marked “GS” and “HMJ”	Refrigerate. Do not freeze. Dispense in original bottle. Do not remove desiccant. Protect from light. Protect from moisture.

^a KADCYLA (ado-trastuzumab emtansine) [package insert]. Genentech, Inc.; July 2014.

^b GILOTRIF (afatinib dimaleate) [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc.; November 2013.

^c ZYKADIA (ceritinib) [package insert]. Novartis Pharmaceuticals Corporation; April 2014.

^d TAFINLAR (dabrafenib) [package insert]. GlaxoSmithKline; January 2014.

^e OPDIVO (nivolumab) [package insert]. Bristol-Myers Squibb Company; March 2015.

^f LYNPARZA (olaparib) [package insert]. Patheon Pharmaceuticals, Inc.; December 2014.

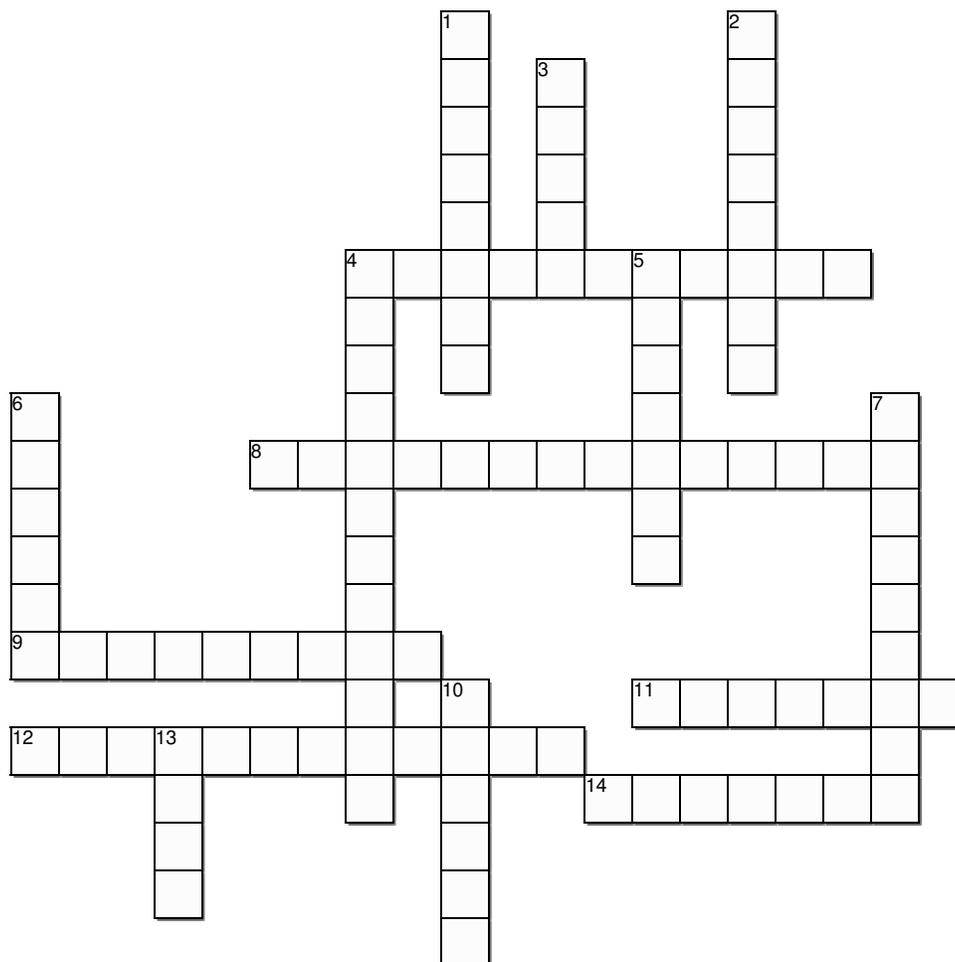
^g KEYTRUDA (pembrolizumab) [package insert]. Merck & Co., Inc.; September 2014.

^h CYRAMZA (ramucirumab) [package insert]. Eli Lilly and Company; April 2014.

ⁱ MEKINIST (trametinib) [package insert]. GlaxoSmithKline; January 2014.

New Drugs Crossword Puzzle C

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

4. Obinutuzumab (GAZYVA) has a black box warning for _____ multifocal leukoencephalopathy.
8. The newest parenteral iron product is ferric _____ (INJECTAFER).
9. Idelalisib is used in combination with _____ (RITUXAN).
11. Pomalidomide (POMALYST) can cause birth _____.
12. Blinatumomab (BLINCYTO) is indicated in _____ chromosome-negative acute lymphoblastic leukemia.
14. Olaparib (LYNPARZA) is approved for _____ cancer.

Down

1. Dabrafenib (TAFINLAR), trametinib (MEKINIST), pembrolizumab (KEYTRUDA), and nivolumab (OPDIVO) are approved for use in late-stage _____.
2. INJECTAFER is administered by intravenous _____ or intravenous "push" injection.
3. Ibrutinib (IMBRUVICA) is administered with a glass of _____.
4. Blinatumomab (BLINCYTO) must be administered through a(n) _____ electronic ambulatory infusion pump.
5. Ramucirumab (CYRAMZA) is approved for _____ cancer.
6. Ado-trastuzumab (KADCYLA) is administered through a 0.22 micron _____.
7. Ado-trastuzumab (KADCYLA) should NOT be confused with trastuzumab (_____).
10. Ibrutinib (IMBRUVICA) tablets should not be crushed or _____.
13. Afatinib (GILOTRIF) and ceritinib (ZYKADIA) are approved for _____ cancer.

Answers on page 54.

(ZYVOX); and oritavancin to be equivalent to a 10-day treatment with vancomycin. Both of these new antibiotics are long acting and have novel administration frequencies as compared with the older glycopeptides.^{119,120}

Dalbavancin is given in a two-dose regimen, 1,000 mg intravenously over 30 minutes, followed by a 500 mg intravenous 30-minute infusion in 7 days. Doses are decreased in kidney disease. The drug is reconstituted with sterile water and diluted with dextrose 5% in water ONLY to a final concentration of 1 to 5 mg/mL. It is not compatible with saline solutions. The reconstituted and diluted product has a beyond-use date of 48 hours at room temperature or refrigerated. Serious adverse effects can include hypersensitivity, rapid infusion reactions, liver enzyme elevations, *C. difficile*-associated diarrhea, and drug-resistant bacteria. Oritavancin is administered as one dose only, 1,200 mg intravenously over three hours. Each 400mg vial is reconstituted with sterile water for injection and further diluted in dextrose 5% in water ONLY to a total volume of 1,000 mL (1.2 mg/mL). Diluted oritavancin has a beyond-use date of 6 hours at room temperature and 12 hours refrigerated. Therapeutic heparin should not be given within 48 hours of an oritavancin dose. Patients should be monitored carefully if oritavancin is given to a patient on warfarin. Serious adverse effects include hypersensitivity, infusion-related reactions, *C. difficile*-associated diarrhea, and osteomyelitis. Dalbavancin and oritavancin are **incompatible** with normal saline, forming a precipitate. If line flushing is done prior to and after dose infusion, it should be done with dextrose 5% in water.^{121,122} Remember that heparin flushes include saline and should NOT be used when either dalbavancin or oritavancin are present in the administration set.

Tedizolid (SIVEXTRO) is an oxazolidinone, as is linezolid (ZYVOX). Oxazolidinones inhibit microbe cell wall synthesis and are considered to be bacteriostatic (prevents bacterial growth – does not kill the bacteria). Clinical trials found that tedizolid given orally for six days was equally effective as linezolid given orally for ten days. Intravenous tedizolid for one day, followed by five days of oral tedizolid was found to work as well as intravenous linezolid for one day followed by nine days of oral linezolid. The dose is 200 mg orally or intravenously over one hour every 24 hours for six days. If administered intravenously, the drug is reconstituted with sterile water for injection and diluted with 250 mL normal saline for a beyond-use date of 24 hours at room temperature or refrigerated. Serious adverse effects include neutropenia, *C. difficile*-associated diarrhea, and drug-resistant bacteria.¹²³

All three of these drugs are effective treatment options for ABSSSI. Unlike vancomycin, blood level monitoring is not needed. Dalbavancin and oritavancin may allow for the outpatient treatment of previously hospitalized patients. However, their long duration could result in prolonged adverse reactions. Daily tedizolid may be more convenient than twice daily linezolid. At this time, the usefulness of these antibiotics in lung or blood stream infections is not known. The cost (WAC) of one week's treatment with dalbavancin is about \$2,980, with oritavancin \$2,900, and with tedizolid \$1,410. Compare this to a week's treatment of vancomycin at about \$140 (WAC).^{124,125}

Complicated Intra-abdominal and Urinary Tract Infections

Complicated intra-abdominal infections (cIAI) are associated with abscesses or infections of the peritoneum – the space in which the intestines lie. Appendicitis (an infection of the appendix) affects about 300,000 patients annually and accounts for 11 million hospital days. The second most common cause of death in the intensive care unit (ICU) that is due to infection is cIAI. Because of where the infection is located anatomically, cIAI must be covered for gram-negative and gram-positive infective organisms.¹²⁶ Complicated urinary tract infections (cUTI) are associated with a structural or functional abnormality in the urinary tract. These may be caused by a wide variety of gram-negative and gram-positive organisms, as well as fungi.¹²⁷

Ceftolozane/tazobactam (ZERBAXA, approved 12/19/14) is a fourth-generation cephalosporin combined with a beta-lactamase inhibitor to protect the cephalosporin from destruction by microbial enzymes. It is indicated in adults for the treatment of cUTI and pyelonephritis (infection of the kidney) and with metronidazole (FLAGYL) for cIAI caused by gram-negative infections. In clinical trials, ceftolozane/tazobactam was found to be equivalent to levofloxacin (LEVAQUIN) in the treatment of cUTI; and to meropenem (MERREM) in the treatment of cIAI. Ceftolozane/tazobactam does not work as well in kidney disease. Adverse effects can include hypersensitivity, *C. difficile*-associated diarrhea, nausea, diarrhea, headache, and fever. The drug is reconstituted with sterile water for injection or normal saline. The reconstituted vial has a beyond-use date of 1 hour. It is further diluted in 100 mL normal saline or dextrose 5% in water for a beyond-use date of 24 hours at room tem-

perature and 7 days refrigerated. The dose is 1.5 grams (1 gram ceftolozane / 0.5 gram tazobactam) given intravenously over one hour every eight hours. The duration of therapy in cIAI is 4 to 14 days, while the duration in cUTI is 7 days. The cost of one week's therapy is about \$1,750 (WAC).^{128,129,130} A recent safety communication warned of medication errors occurring with ZERBAXA due to individual drug strength listing on the packaging. This differs from similar products in which the dose is listed as a sum of the individual drug strengths.¹³¹ Be particularly vigilant when interpreting ZERBAXA's dose and preparation at the time of compounding!

Hepatitis C Virus

According to the CDC, about 3.9 million people in the US are infected with hepatitis C and 2.7 million have active disease. This is an infection caused by the hepatitis C virus (HCV) that can cause liver inflammation (cirrhosis), leading to decreased liver function and possibly liver failure. It is the leading cause of hepatic cancer in the US. About 30,000 new cases are identified each year, and about 8,000-10,000 die from this condition annually. Unfortunately, most people with hepatitis don't have symptoms until liver damage has already occurred. HCV has six different genetic types, with 75% of all US infections caused by genotype 1a or 1b. The medical cost of HCV in the US is about \$600 million annually. The goals of treatment for HCV are to achieve a sustained virologic response (SVR) and to prevent the progression of disease to cirrhosis and hepatic cancer. Treatment options have evolved significantly in recent years and include pegylated interferon, ribavirin, protease inhibitors, and polymerase inhibitors.¹³²

In 2013, two new antiviral drugs for HCV were approved; **simeprevir** (OLYSIO, approved 11/22/13) and **sofosbuvir** (SOVALDI, approved 12/6/13). **Simeprevir** (OLYSIO) is the third protease inhibitor to have been approved and is administered with interferon and ribavirin (REBETOL, COPEGUS) for twelve weeks. Protease inhibitors block HCV's ability to replicate. Simeprevir was evaluated in combination with peginterferon and ribavirin where 80% of patients achieved a sustained virological response on the triple combination in comparison to 40-50% in the peginterferon-ribavirin group. If effective, it is continued for 12 to 36 more weeks. Decreased efficacy was seen in HCV genotype 1a and the product has multiple drug interactions. Serious adverse effects include low heart rate if taken with amiodarone and sofosbuvir, liver failure, rash, photosensitivity (sensitivity to

light), itching, and nausea. Patients should protect themselves from the sun when on this drug. This drug is in Pregnancy Category C. The dose is 150 mg daily by mouth. A course of treatment costs \$40,000-\$73,000 (WAC), depending on the regimen.^{133,134} Sofosbuvir (SOVALDI) is the first polymerase inhibitor approved for HCV and is considered a "game changer." It has activity against all HCV genotypes (1 through 6). Clinical trials showed sustained virological responses in patients treated in combination with peginterferon and ribavirin, those co-infected with HIV, and in patients with liver cancer awaiting transplant. The dose is 400 mg daily by mouth with or without food. For genotypes 1 and 4, it is administered with interferon and ribavirin for 12 weeks. For genotypes 2 and 3, it is given with ribavirin (without interferon) for 12 or 24 weeks, depending on genotype. Sofosbuvir has a significant number of drug interactions. Adverse effects to sofosbuvir alone include headache and tiredness. The cost for 12 weeks therapy is approximately \$84,000 (WAC).^{135,136} In April 2014, the FDA granted approval for the combination of once daily simeprevir with sofosbuvir in the treatment of genotype 1 HCV infection.¹³⁷ Unfortunately, the cost of this combination therapy is over \$150,000 (WAC) for 12 weeks of treatment.

Two new combination products for HCV were approved in 2014; **ledipasvir/sofosbuvir** (HARVONI, approved 10/10/14) and **ombitasvir/paritaprevir/ritonavir/dasabuvir** (VIEKIRA PAK, approved 12/19/14). HARVONI is indicated for genotype 1 chronic hepatitis C and is taken without interferon or ribavirin. Clinical trials in over 1,500 patients showed a sustained viral response of 94% after 8 weeks of treatment and 96% after 12 weeks. Patients who were not previously treated and did not have cirrhosis had a sustained viral response of 99% after 12 weeks. This is a significant advancement in the treatment of the most common and most resistant HCV genotype in the US. Adverse reactions include fatigue, headache, nausea, vomiting, and insomnia. The dose is one tablet (90 mg ledipasvir and 400 mg sofosbuvir) daily by mouth, with or without food, for 12 weeks. Previously treated patients with cirrhosis take the combination for 24 weeks. Untreated patients with lower viral loads can be treated for a shorter duration of 8 weeks. As with the other antiviral drugs, HARVONI has multiple drug interactions. The cost of therapy for 12 weeks is \$94,500 (WAC).^{138,139} VIEKIRA PAK is a four-drug product that includes a triple-combination tablet containing 12.5 mg ombitasvir, 75 mg paritaprevir, and 50 mg ritonavir; and a single-drug tablet containing 250 mg dasabuvir. Ritonavir in the combination tablet increases the blood concentration of

paritaprevir, also included in the combination dose. Patients with genotype 1a or those with cirrhosis take the four-drug combination with ribavirin. Remember that ribavirin is toxic to a fetus. Clinical trials in over 2,000 patients revealed a sustained viral response of 90-100%. In patients without cirrhosis, two triple-combination tablets are taken each morning by mouth, and one dasabuvir tablet is taken twice daily by mouth, one in the morning and one in the evening. Adverse effects include liver enzyme increases, tiredness, itching, nausea, and sleeplessness. This combination product should not be taken with simvastatin (ZOCOR) and has many drug interactions. The cost of 12 weeks therapy is \$83,900 (WAC).^{140,141}

Human Immunodeficiency Virus

Human Immunodeficiency Virus (HIV) is a blood-borne viral infection that damages the immune system. It can be transmitted sexually, through shared intravenous needles or syringes, or from mother to child. In 2006, there were more than 1.1 million Americans infected with HIV. Untreated, the disease has a greater than 90% death rate. The goal of treatment is to prevent the decline of the patient's immune system. Treatment options include highly active antiretroviral therapies (HAART) that use multi-antiretroviral combinations, each of which uses a different mechanism of action to combat HIV. Antiretroviral drugs currently include nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), a fusion inhibitor, a cellular chemokine receptor (CCR5) antagonist, and integrase strand inhibitors.¹⁴²

Dolutegravir (TIVICAY, approved 8/12/13) is an integrase strand inhibitor that is taken in combination with other antiretroviral drugs. It may be used in both adults and children 12 years old and older. Clinical trials showed that patients treated with dolutegravir were less likely to develop treatment resistance than those treated with raltegravir (ISENTRESS). All patients were on a recommended four-drug regimen for HIV. Adverse effects include hypersensitivity, abnormal liver function, headache, and difficulty sleeping. The dose is 50 mg once daily by mouth, with or without food, as one drug of a four-drug regimen. There are many drug interactions. The cost for one month's treatment is about \$1,200 (WAC).^{143,144}

Miscellaneous Anti-Infectives

Peramivir (RAPIVAB, approved 12/22/14) is an influenza (flu) virus neuraminidase inhibitor and is indicated in the treatment of the flu in adults who have shown symptoms for no more than two days. It is the third neuraminidase inhibitor that has been approved, but the first that is administered intravenously. Previously approved neuraminidase inhibitors include oseltamivir (TAMIFLU) and zanamivir (RELENZA). Oseltamivir is an oral drug, and zanamivir is inhaled. Older drugs previously used for the flu are no longer recommended because of increased resistance. In a clinical trial, patients experienced resolution of symptoms 21 hours earlier with peramivir than with placebo. Unfortunately, it could not be determined whether patients who require hospitalization would benefit from this new treatment. After dilution in 100 milliliters of normal saline, half normal saline, dextrose 5% in water or lactated Ringer's, peramivir is administered as a single 600 mg (three 200 mg / 2 mL vials) intravenous dose over 15-30 minutes. Peramivir should be used in those who are unable to take oral or inhaled medications. The most common side effect is diarrhea. Serious side effects include severe skin reactions and neuropsychiatric events. Neuraminidase inhibitors should not be used as a substitute for annual influenza vaccination. A 3-vial dose of peramivir costs \$950 (WAC).^{145,146,147}

Leishmaniasis is a tropical disease caused by a protozoan parasite transmitted by an insect bite. The disease can present itself as ulcers in the throat and nose (mucosal); a large ulcer that involves the skin and structures below it (cutaneous); or a severe disseminated multi-organ illness (visceral). Leishmaniasis is rare in the US. Most cases are contracted during travel or military service abroad. Treating the more severe forms of the disease is a challenge. **Miltefosine** (IMPAVIDO, approved 3/19/14) is indicated for visceral, cutaneous, and mucosal leishmaniasis in patients who are 12 years old or older. Safety and efficacy were established in four clinical trials. Cutaneous trials were done in Columbia and Guatemala, where 66% of patients had resolved ulcers in comparison to 30% of those who took placebo. Mucosal infection was studied in Bolivia, where 62% had complete disease resolution. Visceral leishmaniasis was evaluated in India, where 94% of patients treated with miltefosine and 97% of patients treated with amphotericin B were considered cured. Prescribing information includes a black box warning for fetal toxicity. Women should use effective contraception during treatment and for five months after miltefosine discontinuation. The dose is 50 mg by mouth twice or three times daily for 28 days, depending on patient weight. It should be taken with food. Adverse effects include

nausea, vomiting, diarrhea, headache, dizziness, abdominal pain, decreased appetite, itching, increased liver enzymes, increased creatinine, and sleepiness.^{148,149,150}

Two topical solutions containing antifungal drugs were approved in 2014 for the treatment of toenail fungal infections; **efinaconazole** (JUBLIA, approved 5/23/14) and **tavaborole** (KERYDIN, approved 7/7/14). Efinaconazole (JUBLIA) is available as a 10% solution with a brush applicator. In clinical trials, 15% of patients treated with efinaconazole and 5% treated with placebo achieved a cure after one year. Two drops are applied to an affected big toenail and one drop is applied to other affected toenails once daily for 48 weeks. Drops should be spread to cover the entire nail, the cuticle, and the skin to the side of the nail using the brush provided. The cost for one month's treatment with efinaconazole is \$450 (WAC). Tavaborole (KERYDIN) is available as a 5% solution with a pointed tip dropper. It should be discarded within 3 months of insertion of the dropper and kept away from heat and flame since it contains an alcohol base. Clinical trials showed 6-9% patients treated with tavaborole achieved cure at one year, compared with 0.5-1.5% for those treated with placebo. The solution is applied to the entire surface and under the tip of affected toenails once daily for 48 weeks. Nails should be clean and dry prior to application of either product. Adverse effects for both products include ingrown toenails and application site reactions.^{151,152} See **Table 13 (page 32)**.

Vaccines

Four vaccines were approved in 2013 and 2014. All require provision of a Vaccine Information Sheet to the patient. These can be obtained from the CDC website. A trivalent **influenza vaccine** (FLUBLOK, approved 1/16/13) indicated in 18 to 49 year-olds is produced using recombinant DNA technology, which lends to a faster manufacturing process. It does not contain egg proteins, antibiotics, preservatives or latex. The dose is 0.5mL intramuscularly (IM) given in the deltoid muscle. The cost is \$30 (WAC) per dose.¹⁵³ An **avian influenza vaccine** (Influenza A H5N1 virus monovalent vaccine, adjuvanted, approved 11/22/13) using an egg-based manufacturing process was made for the National Stockpile. The World Health Organization states that the "bird flu" has pandemic potential where 60% of those infected would die. This product will not be available for commercial use. It will be administered in 2 doses, 21 days apart.¹⁵⁴ **Meningococcal group B vaccine** (TRUMENBA, approved 10/29/14) is indicated in 10 to 25 year-olds to combat recent college out-

breaks of meningitis. Until now, there was no vaccine against serogroup B meningitis. There are five major serogroups (A, B, C, Y and W) that cause *N. meningitidis* disease. In 2013, there were 500 cases of meningococcal disease and 20% of those were caused by serogroup B. In clinical trials, 2,800 teens were given three 0.5 milliliter intramuscular doses at 0, 2 and 6 months. Eighty-four percent (84%) of those in the trial generated adequate antibody levels. The duration of protection is currently not known. Adverse effects included injection site reactions, headache, diarrhea, muscle pain, tiredness, and chills. The cost for the 3-dose regimen is \$345 (WAC).^{155,156} A new human papillomavirus (HPV) vaccine contains 5 more HPV types than the original vaccine. **Human papillomavirus 9-valent vaccine** (GARDASIL-9, approved 12/10/14) is indicated in 9 to 26 year-old females for the prevention of cervical, vulvar, vaginal and anal cancer caused by HPV; and in 9 to 15 year-old males for the prevention of anal cancer caused by HPV. Clinical trials conducted in 14,000 females and 1,200 males generated 97% efficacy based on antibody response. The dose is three 0.5 milliliter intramuscular injections at 0, 2, and 6 months. Adverse effects include allergic reactions, fainting, injection site reactions and headache. The cost for one series is about \$500 (WAC).^{157,158} See **Table 14 (page 33)**.

Orphan Drugs

In 2013, the FDA approved 9 new orphan drugs (ADEMPAS, GAZYVA, GILOTREF, IMBRUVICA, KYNAMRO, MEKINIST, OPSUMIT, POMALYST, and TAFINLAR).¹⁵⁹ In 2014, the FDA approved 17 new orphan drugs (BELEODAQ, BLINCYTO, CERDELGA, CYRAMZA, ESBRIET, HETLIOZ, IMPAVIDO, KEYTRUDA, LYNPARZA, MYALEPT, NORTHERA, OFEV, OPDIVO, SYLVANT, VIMIZIM, ZYDELIG, and ZYKADIA.)¹⁶⁰ By definition, orphan drugs are those that treat rare diseases or conditions that affect fewer than 200,000 people in the US. In some cases, new drugs may get orphan drug designation if the disease treated affects more than 200,000 people, but the company is not expected to recoup the costs of developing the drug.

As in previous sections, the rare disease will be briefly described, followed by the approved drug and details important to pharmacy technicians involved in the purchase, storage, and dispensing of these novel new drugs.

Table 13. New Drugs for Infectious Diseases

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Ceftolozane/Tazobactam (ZERBAXA) ^a <i>Approved 12/19/14</i>	Powder for injection	67919-030-01	1 gm ceftolozane / 0.5 gm tazobactam single-dose vials (10)	Refrigerate. Protect from light.
Dalbavancin (DALVANCE) ^b <i>Approved 5/23/14</i>	Lyophilized powder for injection	57970-100-01	500 mg single-dose vial	Store at room temperature.
Dolutegravir (TIVICAY) ^c <i>Approved 8/12/13</i>	Oral tablets	49702-228-13	50 mg yellow round tablets (30) >> marked "SV 572" and "50"	Store at room temperature.
Efinaconazole (JUBLIA) ^d <i>Approved 5/23/14</i>	Topical solution	0187-5400-04 0187-5400-08	4 mL 10% topical solution 8 mL 10% topical solution	Store at room temperature. Flammable, keep away from heat/flames. Do not freeze, store upright. Keep tightly closed.
Ledipasvir/Sofosbuvir (HARVONI) ^e <i>Approved 10/10/14</i>	Oral tablets	61958-1801-1	90 mg ledipasvir / 400 mg sofosbuvir orange diamond-shaped tablets (28) >> marked "GSI" and "7985"	Store at room temperature. Dispense in original container.
Miltefosine (IMPAVIDO) ^f <i>Approved 3/19/14</i>	Oral capsules	61744-050-01	50 mg red capsules blister cards (2x14)	Store at room temperature. Protect from moisture. Dispense in original container.
Ombitasvir/Paritaprevir/ Ritonavir+Dasabuvir (VIEKIRA PAK) ^g <i>Approved 12/19/14</i>	Oral tablets	0074-3093-28	Daily Dose packs (28), each containing: 12.5 mg ombitasvir, 75 mg paritaprevir, 50 mg ritonavir pink oblong tablets (2) >> marked "AV1" 250 mg dasabuvir beige oval tablets (2) >> marked "AV2"	Store at room temperature.
Oritavancin (ORBACTIV) ^h <i>Approved 8/6/14</i>	Lyophilized powder for injection	65293-004-01 65293-004-03	400 mg single-dose vial (1) 400 mg single-dose vial (3)	Store at room temperature.
Peramivir (RAPIVAB) ⁱ <i>Approved 12/22/14</i>	Solution for injection	61364-181-01 61364-181-03	200 mg / 20 mL single-use vial (1) 200 mg / 20 mL single-use vial (3)	Store at room temperature.
Simeprevir (OLYSIO) ^j <i>Approved 11/22/13</i>	Oral capsules	59676-225-28 59676-225-07	150 mg white capsules (28) 150 mg white capsules (7) >> marked "TMC435 150"	Store at room temperature in original container. Protect from light.
Sofosbuvir (SOVALDI) ^k <i>Approved 12/6/13</i>	Oral tablets	61958-1501-1	400 mg yellow oblong tablets (28) >> marked "GSI" and "7977"	Store at room temperature. Dispense in original container.
Tavaborole (KERYDIN) ^l <i>Approved 7/7/14</i>	Topical solution	55724-111-21 55724-111-11	5% topical solution 4 mL with dropper 5% topical solution 10 mL with dropper	Store at room temperature. Flammable, keep away from heat/ flames.
Tedizolid (SIVEXTRO) ^m <i>Approved 6/20/14</i>	Lyophilized powder for injection; oral tablet	67919-040-01 67919-041-01 67919-041-02	200 mg single-use vials (10) 200 mg yellow oval tablets (30) 200 mg yellow oval tablets blister pack (6)	Store at room temperature.

^a ZERBAXA (ceftolozane/tazobactam) [package insert]. Cubist Pharmaceuticals U.S.; December 2014.

^b DALVANCE (dalbavancin) [package insert]. Durata Therapeutics U.S.; May 2014

^c TIVICAY (dolutegravir) [package insert]. GlaxoSmithKline; December 2014.

^d JUBLIA (efinaconazole) [package insert]. Valeant Pharmaceuticals North America LLC; February 2015.

^e HARVONI (ledipasvir/sofosbuvir) [package insert]. Gilead Sciences, Inc.; March 2015.

^f IMPAVIDO (miltefosine) [package insert]. Paladin Therapeutics, Inc.; March 2014.

^g VIEKIRA PAK (ombitasvir, paritaprevir, ritonavir, dasabuvir) [package insert]. AbbVie, Inc.; March 2015.

^h ORBACTIV (oritavancin) [package insert]. The Medicines Company; August 2014.

ⁱ RAPIVAB (peramivir) [package insert]. BioCryst Pharmaceuticals, Inc.; December 2014.

^j OLYSIO (simeprevir) [package insert]. Janssen Therapeutics; April 2015

^k SOVALDI (sofosbuvir) [package insert]. Gilead Sciences, Inc.; March 2015

^l KERYDIN (tavaborole) [package insert]. Anacor Pharmaceuticals, Inc.; February 2015

^m SIVEXTRO (tedizolid) [package insert]. Cubist Pharmaceuticals, Inc.; March 2015.

Table 14. New Vaccines

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
H5N1 avian influenza adjuvanted vaccine ^a <i>Approved 11/22/13</i>	Emulsion for injection	58160-804-01 58160-802-02 58160-808-15 58160-804-15 58160-802-16	H5N1 antigen vial (1) AS03 adjuvant vial (1) H5N1 antigen vials (50) and AS03 adjuvant vials (2x25) H5N1 antigen vials (50) AS03 adjuvant vials (25)	Refrigerate. Do not freeze. Protect from light. Once combined, store under refrigeration for up to 24 hours. National Stockpile.
Human papillomavirus 9-valent vaccine (GARDASIL-9) ^b <i>Approved 12/10/14</i>	Suspension for injection	0006-4119-02 0006-4119-03 0006-4121-02	0.5 mL single-dose vial (1) 0.5 mL single dose vials (10) 0.5 mL single-dose prefilled syringe (10)	Refrigerate. Do not freeze. Protect from light.
Influenza vaccine (FLUBLOK) ^c <i>Approved 1/16/13</i>	Solution for injection	42874-014-10	0.5 mL single-dose vial (10)	Refrigerate. Do not freeze. Protect from light.
Neisseria meningitidis serogroup B vaccine (TRUMENBA) ^d <i>Approved 10/29/14</i>	Suspension for injection	0005-0100-05 0005-0100-10	0.5 mL single-dose prefilled syringe (5) 0.5 mL single-dose prefilled syringe (10)	Refrigerate. Store horizontally. Do not freeze.

^a Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted [package insert]. GlaxoSmithKline; November 2013
^b GARDASIL-9 (Human papillomavirus 9-valent vaccine) [package insert]. Merck & Co., Inc.; February 2015.
^c FLUBLOK (Influenza vaccine) [package insert]. Protein Sciences Corporation; October 2014.
^d TRUMENBA (meningococcal group B vaccine) [package insert]. Wyeth Pharmaceuticals, Inc.; October 2014.

Cystic Fibrosis (CF)

Cystic Fibrosis (CF) is an inherited condition in which a defective gene results in thickened mucus in the lungs, pancreas, gastrointestinal tract, and sweat glands. This results in chronic lung and pancreatic disease. About 30,000 children and adults in the US are affected by CF. Individuals with CF are very susceptible to lung infection caused by *Pseudomonas aeruginosa*. Although not a new drug, the **tobramycin inhaler** (TOBI PODHALER, approved 3/22/13) represents an important new way to deliver tobramycin into the lungs of CF patients. Prior to the introduction of this product, tobramycin inhalation treatments were only available by nebulizer. Clinical trials showed equivalence between the PODHALER and nebulizer methods of administration. Additionally, the PODHALER took a much shorter time to administer. The dose is four 28 mg inhalation capsules twice daily for 28 days by PODHALER device, after which the patient is off the treatment for 28 days before starting again. The powder contents of the inhalation capsules are inhaled one at a time. Capsules should be stored in the blister provided and only removed immediately before use. The cost of one 28-day treatment cycle by inhaler or nebulizer is the same, about \$6,700 (WAC).^{161,162,163}

Pulmonary Arterial Hypertension (PAH)

Pulmonary Arterial Hypertension (PAH) is a condition in which the arterial blood pressure in the lungs is high, making it harder for the heart to pump blood. This is a progressive disease that often leads to lung transplantation to prevent inevitable death. Two drugs were approved in 2013 to treat PAH. **Riociguat** (ADEMPAS, approved 10/8/13) is a soluble guanylate cyclase (sGC) stimulator that relaxes arteries to allow for a decrease in blood pressure and an increase in blood flow. People on riociguat in clinical trial were able to walk 150 feet further than those who were given placebo. This drug may not be administered to pregnant women and can only be obtained through a certified pharmacy. The dose is 1 mg three times daily by mouth and can be increased by 0.5 mg every 2 weeks up to 2.5 mg three times daily. Adverse drug reactions include headache, dizziness, edema, nausea, diarrhea, and vomiting. Smokers may require higher doses and patients should not take antacids within 1 hour of taking this drug. The cost for one month's treatment is \$7,500 (WAC).^{164,165} **Macitentan** (OPSUMIT, approved 10/18/13) is the second nonselective endothelin receptor blocker and a derivative of bosentan (TRACLEER). In clinical trials, it delayed disease progression as compared with

placebo. Adverse effects include anemia, headache, influenza, upper respiratory tract infection, and urinary tract infection. While it was shown to decrease morbidity, the claim to decrease mortality is misleading. The drug may not be given to pregnant women due to fetal toxicity. The dose is 10 mg once daily by mouth. The cost for one month's treatment is \$6,900 (WAC).^{166,167} Riociguat and macitentan were approved with REMS medication guides, elements to assure safe use, and implementation systems that inform patients and prescribers of the product's risks.⁶⁶

Idiopathic Pulmonary Fibrosis (IPF)

Idiopathic pulmonary fibrosis (IPF) is a lung condition in which tissue becomes scarred, leading to shortness of breath, cough, and an inability to take part in normal physical activity. The disease occurs in adults 50 years old and older and results in survival of about three years. Treatment includes oxygen, lung rehabilitation, and lung transplant. After transplant, 5-year survival is 44%. Two drugs were approved in 2014 to treat IPF. **Pirfenidone** (ESBRIET, approved 10/15/14) has been available in Europe since 2011 and in Canada since 2012. Pirfenidone works by multiple mechanisms to decrease lung tissue scarring and to decrease the decline in the amount of air exhaled in a deep breath. The dose of pirfenidone is initially 267 mg taken three times daily for seven days, then 534 mg (two 267 mg capsules) three times daily for seven days, and finally 801 mg (three 267 mg capsules) three times daily. Pirfenidone should be taken with food. **Nintedanib** (OFEV, approved 10/15/14) is a kinase inhibitor that blocks lung tissue scarring by several mechanisms and decreases the decline in the amount of air that can be expelled in a deep breath. The dose of nintedanib is 150 mg twice daily with food. The cost for each of these drug products is about \$8,000 (WAC) for a month's supply. Benefit from therapy for those with severe disease has not been established.^{168,169,170}

Non-24-hour Sleep-wake Disorder (Non-24)

Non-24-hour sleep-wake disorder (non-24) is a condition in which completely blind persons suffer from insomnia because their daily sleep cycle is not interrupted by the light-dark cycle that signals sighted people to a 24-hour sleep-wake cycle. As a result, blind people can have longer sleep-wake cycles than 24 hours. This causes insomnia at night and sleepiness during the day. **Tasimelteon** (HETLIOZ, approved 1/31/14) is a melatonin receptor agonist that affects sleep and the daily sleep-wake cycle. In people

with sight, melatonin levels increase during the night and are decreased during the day. Tasimelteon may therefore act by signaling the body that it is nighttime. During clinical trials, 20% of those taking tasimelteon were able to get day-night synchronized as compared to only 3% of those taking placebo. The dose is 20 mg by mouth one hour prior to bedtime daily. The drug is taken without food. It may take weeks for the person to get benefit from the drug. Adverse effects include headache, elevated liver enzymes, and unusual dreams. The cost of one month's treatment is \$7,020 (WAC). It is not known how this drug compares to taking a melatonin supplement.^{171,172}

Neurogenic Orthostatic Hypotension (NOH)

Neurogenic Orthostatic Hypotension (NOH) is a rare condition in which a person faints upon standing. The condition is associated with Parkinson's disease and with autonomic nervous system failure. Individuals with this condition do not have the ability to do normal activities that require standing or walking. **Droxidopa** (NORTHERA, approved 2/18/14) is a synthetic amino acid that is converted to norepinephrine. Prescribing information includes a black box warning about the risk of high blood pressure when lying down, which can increase the risk of stroke. To decrease the risk of this effect, the head of the bed should be raised and the last daily dose taken no less than three hours before bedtime. The dose is 100 mg three times daily and may be increased by 100 mg to a maximum of 600 mg three times daily.^{173,174}

Hereditary Angioedema (HAE)

Hereditary Angioedema (HAE) is a rare genetic disorder in which those affected have low levels of plasma protein C1 inhibitor (C1-INH). About 6,000 to 10,000 people in the US have HAE. Acute attacks of HAE may be triggered by hormone levels, trauma, and stress. These triggers result in swelling, including airway obstruction or severe abdominal pain. Prior to current therapies, mortality (death rate) was 20-30% due to the inability to breathe as a result of airway swelling. Preventive treatments now include androgens and replacement C1-INH. Acute treatments include replacement C1-INH, C1-esterase INH, ecallantide (KALBITOR), and icatibant (FIRAZYR). Supportive treatment includes fluid replacement, pain management, intubation, and elimination of triggers. **C1-esterase inhibitor, recombinant** (RUCONEST, approved 7/16/14) is the first recombinant replacement therapy for HAE and has been shown to shorten the duration of HAE

attack over placebo. Adverse events include hypersensitivity, blood clots, headache, nausea, and diarrhea. The drug is reconstituted with sterile water, which is not included in the packaging and must be provided separately. The beyond-use-dating of the reconstituted solution is 8 hours refrigerated. The dose is 50 international units per kilogram (up to 4,200 international units) given by slow intravenous injection over 5 minutes. A second dose can be given if the attack does not subside. Patients can be taught to self-administer the drug, allowing for immediate treatment without having to get to an emergency room. The product is a protein, so it should not be shaken or frozen.^{175,176,177}

Botulism

Botulism is a serious poisoning caused by toxins that are released by certain bacteria. Symptoms include severe muscle weakness that starts from the head and progresses through the rest of the body. If botulism is not treated, it can lead to muscle paralysis and the inability to breathe. **Botulism antitoxin heptavalent** (BAT, approved 3/22/13) is the only product available to treat adults and contains antibodies to all 7 botulism neurotoxins. It is derived from horse serum. A human antitoxin (Baby-BIG) has been available for infants. BAT is administered by slow intravenous infusion after dilution in normal saline and is distributed through the CDC and warehoused in the Strategic National Stockpile.^{178,179}

Generalized Lipodystrophy

Generalized lipodystrophy is a genetic or autoimmune deficiency of leptin, which regulates food intake and insulin. Patients with generalized lipodystrophy have severely high triglycerides, lack of fat tissue, pancreatitis, an enlarged fatty liver, fat stored in muscle (including the heart), a muscular appearance, insulin resistance, a high metabolic rate and increased appetite. There are perhaps 30 individuals in the US and 500 worldwide who have this condition. People with generalized lipodystrophy die from heart failure at an early age. Treatment has included restricting fat intake, and providing type 1 diabetic therapy. **Metreleptin** (MYALEPT, approved 2/25/14) binds to leptin receptors and reinstates informing the central nervous system of the body's fat stores. Prescribing information includes a black box warning about the development of antibodies that can inactivate metreleptin and the risk of lymphoma. Dosing is weight- and gender-based, given once daily by subcutaneous injection, and adjusted to physical response. The drug is reconstituted

with bacteriostatic water for injection to provide a beyond-use date of 3 days if refrigerated. If prepared for infants, sterile water for injection (without bacteriostat) must be used, and unused product must be discarded. The cost of therapy at 5 mg per day is approximately \$250,000 (WAC) annually.^{180,181,182} Metreleptin is only available through a restricted program called MYALEPT REMS PROGRAM to ensure safe use.⁶⁶

Homozygous Familial Hypercholesterolemia (HoFH)

Homozygous familial hypercholesterolemia (HoFH) is an inherited condition in which individuals can't remove low density lipoprotein (LDL) cholesterol from their blood stream. There are perhaps 300 individuals in the US that have inherited this trait from both of their parents. Death from heart attack occurs before 30 years of age and can occur in individuals as young as 1 or 2 years old. **Mipomersen sodium** (KYNAMRO, approved 1/29/13) is a synthetic nucleic acid that decreases the formation of very low density lipoproteins (VLDL) and LDL. It is used in conjunction with diet and lipid-lowering medications. Its effect on the risk of heart attack has not been determined, but it has decreased LDL by as much as 25% from baseline. Prescribing information has a black box warning regarding severe liver toxicity. The drug was not approved in Europe due to its liver toxicity. The dose is 200 mg in a 1 milliliter subcutaneous injection weekly. If liver enzymes increase, the drug is either held or discontinued. The cost of therapy, as stated by the manufacturer, is about \$176,000.^{183,184,185} Mipomersen was approved with a REMS program, is distributed through a limited channel, and requires prescriber certification.⁶⁶

Urea Cycle Disorders (UCDs)

Urea cycle disorders (UCDs) are genetic disorders caused by deficiencies in enzymes that normally remove ammonia from the body. Normally, when protein is consumed, nitrogen is produced, converted to urea, and removed from the body through the urine. People with UCDs are unable to excrete excess nitrogen, which stays in the body as ammonia. Accumulation of ammonia can cause brain damage, coma, and death. **Glycerol phenylbutyrate** (RAVICTI, approved 2/1/13) is an oral liquid that is taken three times daily with low-protein meals. It facilitates the excretion of nitrogen in a different way than through the urea cycle. The initial dose is 4.5 to 11.2 mL/m²/day

divided in three equal doses and taken with meals. Adverse effects include headache, diarrhea, and flatulence. The cost of one 25 milliliter bottle is \$2,500 (WAC).^{186,187}

Mucopolysaccharidosis Type IV-A (MPS IV-A)

Mucopolysaccharidosis type IV-A (MPS IV-A), also known as Morquio A Syndrome is a rare autosomal recessive genetic disorder in which there are inadequate levels of the enzyme N-acetylgalactosamine-6-sulfatase. This deficiency causes the intracellular accumulation of glycosaminoglycans. Individuals with this enzyme deficiency appear healthy at birth, but by 6 years old show chest deformity, altered bone development, frequent lung infections, early coronary heart disease, difficulty walking, and increased weight compared to body size. There are about 800 persons in the US with MPS IV-A. **Elosulfase alfa** (VIMIZIM, approved 2/14/14) is the first enzyme replacement therapy for MPS IV-A. It is a recombinant protein produced in Chinese hamster ovary cells. Clinical trials showed that patients with MPS IV-A after 48 weeks of treatment were able to walk a significantly longer distance (74 feet more) in 6 minutes than those treated with placebo. Prescribing information includes a black box warning for anaphylaxis. Adverse effects include respiratory complications, spinal cord compression, fever, vomiting, headache, nausea, chills, abdominal pain, and tiredness. The drug is approved for individuals 2 years old and older. The dose is 2 mg/kg intravenously over 3.5 to 4.5 hours (depending on the total volume of the solution) weekly. Patients should be pre-treated with an antihistamine. The drug is diluted in normal saline to a final volume of 100 or 250mL, depending on body weight, and has a beyond-use dating of 24 hours at room temperature or refrigerated. It is administered through a 0.2 micron filter. In the event of hypersensitivity, the infusion should be slowed, stopped, or discontinued, as appropriate. The therapy costs about \$380,000 annually.^{188,189}

Gaucher Disease

Gaucher disease is another autosomal recessive genetic disorder. The lack of an enzyme, glucocerebrosidase, results in the buildup of a glycolipid in the liver, spleen, bones, bone marrow, and nervous system. This buildup affects cell function and leads to decreases in all blood cell types (pancytopenia), significant enlargement of the liver and spleen, and altered lung function. There is a wide range of disease severity, and subtypes are categorized based on the extent that the nervous system is affected.

This condition is rare and affects about 6,000 people in the US. Treatment options include enzyme replacement therapy, surgery, and pain management.¹⁹⁰ **Eliglustat** (CERDELGA, approved 8/19/14) is an oral glucosylceramide synthase inhibitor indicated for non-neuropathic Gaucher disease. In clinical trials, patients treated with eliglustat had a greater reduction in spleen size as compared with patients receiving placebo. Reductions in hemoglobin, platelet counts, spleen size, and liver size were similar to those after treatment with the parenteral enzyme replacement therapy imiglucerase (CEREZYME). Adverse reactions include tiredness, headache, nausea, diarrhea, back pain, upper abdominal pain, and pain in the arms and legs. There are significant drug interactions with this medication and it is in Pregnancy Category C. The dose is 84 mg orally once or twice daily, depending on the patient's metabolism profile. Patients can be started on this oral therapy 24 hours after the last dose of enzyme replacement with imiglucerase (CEREZYME), velaglucerase (VPIRV) or taliglucerase alfa (ELELYSO). This oral drug's cost is \$310,000 annually, equivalent to that for CEREZYME.^{191,192}

Miscellaneous Orphan Drugs

Human Prothrombin Complex Concentrate (KCEN-TRA, approved 4/29/13) is a plasma-derived concentrate of factors II, VII, IX, and X used for the reversal of warfarin anticoagulation. The only other product approved for use in the US for warfarin reversal is plasma itself. Both of these products are used with vitamin K to stop the bleeding caused by too high a dose of warfarin. While plasma requires blood typing and thawing, KCEN-TRA does not. For this reason it can be administered much more quickly. Prescribing information carries a black box warning about the risk of blood clots. The cost of treatment is about \$4,500 according to the manufacturer.^{193,194}

Recombinant coagulation factor XIII A-Subunit (TRETEN, approved 12/23/13) is indicated in the prevention of bleeding in patients with Congenital factor XIII A-subunit deficiency, a rare autosomal recessive disorder. There are approximately 100 individuals in the US with this condition. Factor XIII is necessary for normal clotting. When a person with this condition has a bleed into their central nervous system, there is a 50% chance of death. The severity of bleeding varies between families. Adverse effects include hypersensitivity, thromboembolism, and antibodies against TRETEN, headache, injection site pain, arm pain and leg pain. The product is

produced in yeast, so it has no animal components. It is reconstituted with sterile water for injection and must be used within 3 hours. The dose is 35 international units per kilogram administered intravenously over 1-2 mL/min monthly.^{195,196}

Antihemophilic factor, recombinant, Fc fusion protein (ELOCTATE, approved 6/6/14) is the first longer acting factor VIII product for use in adults and children with congenital hemophilia A, which is the most common X-linked recessive disorder. Hemophilia A affects about 20,000 males in the US. The goals of therapy are to manage bleeding episodes, replace factor, treat factor inhibitors, and rehabilitate damaged joints. ELOCTATE is made up of a factor VIII molecule that is fused to a portion of a human IgG immune globulin to delay the degradation of the factor and allow it to stay in the blood stream longer. Adverse effects include hypersensitivity, neutralizing antibodies to ELOCTATE, joint pain, and tiredness. The product can be used in a prophylactic manner (to maintain adequate blood levels of factor VIII) or on-demand (to provide factor VIII when it is needed due to injury or planned surgery)³. Patients and their families learn to self-administer this therapy. Once reconstituted with sterile water, the product must be infused intravenously within 3 hours.^{197,198}

Antihemophilic factor, recombinant, porcine sequence (OBIZUR, approved 10/23/14) is a recombinant pig factor VIII produced by baby hamster kidney cells. It is indicated for adults with *acquired hemophilia A*, a condition in which the patient produces antibodies against their own factor VIII. Pig-derived factor is used because it will be less likely to be blocked by the patient's inhibiting antibodies. Adverse effects include hypersensitivity and neutralizing antibodies to OBIZUR. Patients can be taught to self-administer this treatment. Once reconstituted with sterile water, the product must be used within 3 hours. The initial dose is 200 units per kilogram given intravenously as 1 to 2 milliliters per minute and titrated to factor VIII levels and patient response. The product is five times more expensive than other factor VIII products.^{199,200}

Two Factor IX products for *hemophilia B* were approved in 2013 and 2014; **recombinant coagulation Factor IX** (RIXUBIS, approved 6/27/13) and **recombinant Factor IX, Fc Fusion Protein** (ALPROLIX, approved 3/28/14). Hemophilia B is an X-linked recessive disorder also known as Christmas disease (named after the first diagnosed patient). This condition, a deficiency of functioning clotting factor

IX, accounts for 20% of all hemophilia cases. It affects about 3,300 males in the US. The goals of therapy are to manage bleeding episodes, replace factor, treat factor inhibitors, and rehabilitate damaged joints. RIXUBIS is a recombinant replacement factor IX used on-demand to control bleeding episodes, during the surgery of a hemophilia B patient, or as routine prophylaxis to prevent bleeding episodes. Adverse effects include hypersensitivity, neutralizing antibodies, blood clots, distorted taste, and pain in the arms and legs. The product is stored in the refrigerator, but can be stored at room temperature for up to six months. The product should not be re-refrigerated. Patients are taught to self-administer. Once the product is reconstituted with sterile water, it must be used within 3 hours. The dose is calculated on the basis of how many units are needed to raise the patient's serum factor IX to levels that will decrease the risk of bleeding. Routine prophylaxis is usually dosed at 4 to 60 international units per kilogram twice weekly. ALPROLIX is the first long-acting factor IX product. The factor IX molecule in this product is fused to a portion of a human IgG immune globulin to delay the degradation of the factor and allow it to stay in the blood stream longer. Adverse effects include hypersensitivity, neutralizing antibodies, blood clots, and headache. Patients are taught to self-administer this therapy. Once reconstituted with sterile water for injection, it must be used within 3 hours. Prophylactic (preventive) dosing is 50 to 100 international units per kilogram given intravenously at 10 milliliters per minute every ten days. The dose or frequency can be adjusted. The product can be used for on-demand control of a bleeding episode or to prevent bleeding during surgery.^{201,202,203}

Siltuximab (SYLVANT, approved 4/23/14) is a monoclonal antibody against IL-6 used in the treatment of HIV-negative and human herpesvirus-8 (HHV-8) negative *Multicentric Castleman's Disease* (MCD). This is a rare and complex blood condition that acts like a lymphoma, but is not a cancer. It results in IL-6 overproduction which causes a significant inflammatory response. There are about 1000 MCD cases in the US per year. Survival depends on whether the patient has unicentric disease, multicentric HIV-negative disease, or multicentric HIV-positive disease. The last of these has the poorest prognosis. Treatment includes corticosteroids, antiviral drugs, thalidomide, chemotherapy and monoclonal antibodies. Siltuximab is given at a dose of 11 mg per kilogram intravenously over one hour every three weeks until treatment failure. The cost is \$6,700 (WAC) per treatment.^{204,205,206} See **Table 15** (page 38-40).

Table 15. New Orphan Drugs

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Antihemophilic factor, recombinant, Fc fusion protein (ELOCTATE) ^a <i>Approved 6/6/14</i>	Lyophilized powder for intravenous injection	64406-801-01	~250 IU single-dose vial, SWI syringe, vial adapter, 1 each	Refrigerate. May store at room temperature for 6 months. Do not re-refrigerate. Protect from light. Do not freeze. Reconstituted product can be stored at room temperature for 3 hours.
		64406-802-01	~500 IU single-dose vial, SWI syringe, vial adapter, 1 each	
		64406-803-01	~750 IU single-dose vial, SWI syringe, vial adapter, 1 each	
		64406-804-01	~1,000 IU single-dose vial, SWI syringe, vial adapter, 1 each	
		64406-805-01	~1,500 IU single-dose vial, SWI syringe, vial adapter, 1 each	
		64406-806-01	~2,000 IU single-dose vial, SWI syringe, vial adapter, 1 each	
		64406-807-01	~3,000 IU single-dose vial, SWI syringe, vial adapter, 1 each	
Antihemophilic factor, recombinant, porcine sequence (OBIZUR) ^b <i>Approved 10/23/14</i>	Lyophilized powder for reconstitution	0944-5001-01	~500 units single-use vial, 1 mL SWI syringe, vial adapter with filter, 1 each	Refrigerate. Do not freeze. Protect from light. Use within 3 hours of reconstitution.
		0944-5001-05	~500 units single-use vials, 1 mL SWI syringes, vial adapters with filter, 5 each	
		0944-5001-10	~500 units single-use vials, 1 mL SWI syringe, vial adapter with filter, 10 each	
Botulism antitoxin heptavalent (BAT) ^c <i>Approved 3/22/13</i>	Solution for injection	60492-0075-2	20 mL single-use vial, containing: 4,500 units serotype A antitoxin >3,300 units serotype B antitoxin >3,000 units serotype C antitoxin >600 units serotype D antitoxin >5,100 units serotype E antitoxin >3,000 units serotype F antitoxin >600 units serotype G antitoxin	For Strategic National Stockpile use only. Store frozen. Once thawed, may be refrigerated for 36 months.
		60492-0075-3	50 mL single-use vial, containing above antitoxins	
c1-esterase inhibitor, recombinant (RUCONEST) ^d <i>Approved 7/16/14</i>	Lyophilized powder for reconstitution	68012-350-01	2,100 IU single-use vial (1)	Refrigerate. Protect from light. Do not freeze.
Coagulation factor XIII A-Subunit, recombinant (TRETEN) ^e <i>Approved 12/23/13</i>	Lyophilized powder for reconstitution	0169-7013-11	Single-use vial, amount stated on vial (1)	Refrigerate. Do not freeze. Protect from light. Use within 3 hours of reconstitution.
		0169-7013-01	Single-use vial and SWI vial	
		0169-7000-93	SWI vial	
Coagulation factor IX, recombinant (ALPROLIX) ^f <i>Approved 3/28/14</i>	Lyophilized powder for reconstitution	64406-911-01	500 IU single-use vial, diluent syringe, vial adapter (1 each)	Refrigerate. May be stored in at room temperature for 6 months. Do not re-refrigerate. Protect from light. Do not freeze. Use within 3 hours of reconstitution.
		64406-922-01	1,000 IU single-use vial, diluent syringe, vial adapter (1 each)	
		64406-933-01	2,000 IU single-use vial, diluent syringe vial adapter (1 each)	
		64406-944-01	3,000 IU single-use vial, diluent syringe, vial adapter (1 each)	
Coagulation factor IX, recombinant (RIXUBIS) ^g <i>Approved 6/27/13</i>	Lyophilized powder for reconstitution	0944-3026-02	~250 IU single-use vial, 5 mL SWI, transfer device, 1 each, light blue color code	Refrigerate. May store at room temperature for 12 months. Do not re-refrigerate. Do not freeze.
		0944-3028-02	~500 IU single-use vial, 5 mL SWI, transfer device, 1 each, pink color code	
		0944-3030-02	~1,000 IU single-use vial, 5 mL SWI, transfer device, 1 each, green color code	
		0944-3032-02	~2,000 IU single-use vial, 5 mL SWI, transfer device, 1 each, orange color code	
		0944-3034-02	~3,000 IU single-use vial, 5 mL SWI, transfer device, 1 each, silver color code	

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Droxidopa (NORTHERA) ^h <i>Approved 2/18/14</i>	Oral capsules	76320-100-90 76320-200-90 76320-300-90	100 mg light blue and white capsules (90) >> marked "Northera" and "100" 200 mg lt. yellow and white capsules (90) >> marked "Northera" and "200" 300 mg light green and white capsules (90) >> marked "Northera" and "300"	Store at room temperature.
Eliglustat (CERDELGA) ⁱ <i>Approved 8/19/14</i>	Oral capsules	58468-0220-1 58468-0220-2	84 mg pearl blue-green and white capsules (4x14) 84 mg pearl blue-green and white capsules (1x14) >> marked "GZ02"	Store at room temperature.
Elosulfase alfa (VIMIZIM) ^j <i>Approved 2/14/14</i>	Injection	68135-100-01	5 mg / 5 mL single-use vial (1)	Refrigerate. Do not freeze. Do not shake. Protect from light.
Glycerol phenylbutyrate (RAVICTI) ^k <i>Approved 2/1/13</i>	Oral liquid	76325-100-25 76325-100-04	25 mL, 1.1 Gm/mL oral liquid bottle (1) 25 mL, 1.1 Gm/mL oral liquid bottle (4)	Store at room temperature.
Macitentan (OPSUMIT) ^l <i>Approved 10/18/13</i>	Oral tablets	66215-501-15 66215-501-30	10 mg white tablets blister pack (15) 10 mg white tablets bottle (30) >> marked "10" on one side	Store at room temperature.
Metreleptin (MYALEPT) ^m <i>Approved 2/25/14</i>	Lyophilized cake for reconstitution	66780-310-01	11.3 mg vial (1)	Refrigerate. Protect from light. Do not freeze.
Mipomersen sodium (KYNAMRO) ⁿ <i>Approved 1/29/13</i>	Solution for subcutaneous injection	58468-0190-1 58468-0190-2 58468-0190-1 58468-0190-2	200 mg/mL 1 mL single-use vial (1) 200 mg/mL 1 mL single-use vials (4) 200 mg/mL 1 mL prefilled syringe (1) 200 mg/mL 1 mL prefilled syringe (4)	Refrigerate. May be stored at room temperature for 14 days. Do not re-refrigerate. Protect from light.
Nintedanib (OFEV) ^o <i>Approved 10/15/14</i>	Oral capsules	0597-0145-60 0597-0143-60	100 mg peach soft capsules (60) >> marked "100" and company symbol 150 mg brown soft capsules (60) >> marked "150" and company symbol	Store at room temperature Protect from heat. Protect from humidity.
Pirfenidone (ESBRIET) ^p <i>Approved 10/15/14</i>	Oral capsules	64116-121-01 64116-121-02 64116-121-03	267 mg white capsules bottle (270) 267 mg white capsules blister cards (1 x 21; 1 x 42) 267 mg white capsules blister cards (4 x 63) >> marked "InterMune [®] " and "267 mg"	Store at room temperature. Keep tightly sealed.
Prothrombin complex concentrate, human (KCENTRA) ^q <i>Approved 4/29/13</i>	Lyophilized powder for reconstitution	63833-396-01 63833-761-20 63833-386-02	500 units single-use vial (1) 20 mL SWI vial (1) Above vials, filtered transfer set, alcohol swab	Store refrigerated or room temperature. Do not freeze. Protect from light.
Riociguat (ADEMPAS) ^r <i>Approved 10/8/13</i>	Oral tablets	50419-250-03 50419-250-01 50419-251-03 50419-251-01 50419-252-03 50419-252-01 50419-253-03 50419-253-01 50419-253-03 50419-253-01	0.5 mg white round tablets (42) 0.5 mg white round tablets (90) >> marked "0.5 R" and Bayer cross 1 mg pale yellow round tablets (42) 1 mg pale yellow round tablets (90) >> marked "1 R" and Bayer cross 1.5 mg yellow-orange round tablets (42) 1.5 mg yellow-orange round tablets (90) >> marked "1.5 R" and Bayer cross 2 mg pale orange round tablets (42) 2 mg pale orange round tablets (90) >> marked "2 R" and Bayer cross 2.5 mg red-orange round tablets (42) 2.5 mg red-orange round tablets (90) >> marked "2.5 R" and Bayer cross	Store at room temperature.

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Siltuximab (SYLVANT) ^s <i>Approved 4/23/14</i>	Lyophilized powder for reconstitution	57894-420-01 57894-421-01	100 mg single-use vial 400 mg single-use vial	Refrigerate. Protect from light.
Tasimelteon (HETLIOZ) ^t <i>Approved 1/31/14</i>	Oral capsules	43068-220-01	20 mg dark blue capsules (30) >> marked "VANDA 20mg" in white	Store at room temperature. Protect from light. Protect from moisture.
Tobramycin (TOBI PODHALER) ^u <i>Approved 3/22/13</i>	Powder for oral inhalation	0078-0630-35 0078-0630-20 0078-0630-19	28 mg capsule for inhalation blister packs (224, 4x7x8) and 2 Podhaler devices 28 mg capsule for inhalation blister pack (56, 7x8) and 1 Podhaler device 28 mg capsule for inhalation blister pack (8, 1x8) and 1 Podhaler device >> marked "NVR AVCI" & company logo	Store at room temperature. Protect from moisture. Use with Podhaler device only.

^a ELOCTATE (antihemophilic factor recombinant, Fc fusion protein) [package insert]. Biogen Idec, Inc.; June 2014.
^b OBIZUR (antihemophilic factor recombinant, porcine sequence) [package insert]. Baxter Healthcare Corporation; October 2014.
^c BAT (botulism antitoxin heptavalent A, B, C, D, E, F, G, equine) [package insert]. Cangene Corporation; March 2013.
^d RUCONEST (C1 esterase inhibitor, recombinant) [package insert]. Santarus, Inc.; February 2015.
^e TRETEN (coagulation factor XIII A-subunit, recombinant) [package insert]. Novo Nordisk, Inc.; April 2014.
^f ALPROLIX (coagulation factor IX, recombinant, Fc fusion protein) [package insert]. Biogen Idec, Inc.; March 2014.
^g RIXUBIS (coagulation factor IX, recombinant) [package insert]. Baxter Healthcare Corporation; September 2014.
^h NORTHERA (droxidopa) [package insert]. Chelsea Therapeutics, Inc.; February 2014.
ⁱ CERDELGA (eliglustat) [package insert]. Genzyme Corporation; August 2014.
^j VIMIZIM (elosulfase alfa) [package insert]. BioMarin Pharmaceutical, Inc.; February 2014.
^k RAVICTI (glycerol phenylbutyrate) [package insert]. Hyperion Therapeutics, Inc.; June 2014.
^l OPSUMIT (macitentan) [package insert]. Actelion Pharmaceuticals, Inc.; April 2015.
^m MYALEPT (metreleptin) [package insert]. AstraZeneca Pharmaceuticals LP; June 2014.
ⁿ KYNAMRO (mipomersen sodium) [package insert]. Genzyme Corporation; February 2015.
^o OFEV (nintedanib) [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc.; October 2014.
^p ESBRIET (pirfenidone) [package insert]. InterMune, Inc.; October 2014.
^q KCENTRA (prothrombin complex concentrate, human) [package insert]. CSL Behring LLC; April 2013.
^r ADEMPAS (riociguat) [package insert]. Bayer Healthcare; May 2014.
^s SYLVANT (siltuximab) [package insert]. Janssen Biotech, Inc.; June 2014.
^t HETLIOZ (tasimelteon) [package insert]. Vanda Pharmaceuticals, Inc.; December 2014.
^u TOBI PODHALER (tobramycin inhalation powder) [package insert]. Novartis Pharmaceuticals Corporation; March 2015.

Orphan Drug Search

Can you find 30 orphan generic or brand drug names?

N G Q O B I Z U R A R T N E C K I N K T
 E Y S Y A F V C A R E H T R O N J I K A
 T S A T M N I T P E L E R T E M L B F T
 T N P I I Y Z X I X K S Y L V A N T N S
 E D M M X A A R R L W H W E G S E I M U
 R A E U U V L I F N L L R Q I Y N I S L
 T G D S T U P O E L A J F B L T P E V G
 L L A P L F R C N B V T U C E O O T I I
 P E E O I X O I I B Q X N D M I P O M L
 C D T S S K L G D D I R A E Z B H B I E
 U R E X B G I U O R J N R L T I Z I Z L
 Z E K X D R X A N O I S I O P I O H I B
 U C M A L B I T E B E V A S E H C D M E
 E T A T C O L E W N Y E C U L E P A Y R
 R B Y Z Z I I C T G V F G L A T M Q M I
 A P O D I X O R D L W O T F Y L A T R G
 Z M X D O R M A N Y K X Y A M I B R V J
 M T T J R U C O N E S T F S H O P K X M
 X A U J O C Y P A K S O G E J Z G Z V S
 V O W T N O E T L E M I S A T J U C K F

ADEMPAS
 ALPROLIX
 CERDELGA
 DROXIDOPA
 ELIGLUSTAT
 ELOCTATE
 ELOSULFASE
 ESBRIET
 HETLIOZ
 KCENTRA

KYNAMRO
 MACITENTAN
 METRELEPTIN
 MIPOMERSEN
 MYALEPT
 NINTEDANIB
 NORTHERA
 OBIZUR
 OFEV
 OPSUMIT

PIRFENIDONE
 RIOCIGUAT
 RIXUBIS
 RUCONEST
 SILTUXIMAB
 SYLVANT
 TASIMELTEON
 TOBI
 TRETEN
 VIMIZIM

Answers on page 55.

Miscellaneous New Drugs

A soybean and olive oil **lipid injectable emulsion** (CLINOLIPID, approved 10/3/13) was granted priority review to help alleviate the fat emulsion shortages in 2013. Fat emulsion is used as an important source of energy in the provision of parenteral nutrition. Clinical trials showed that CLINOLIPID has similar short term outcomes as soybean oil-derived products already on the market. CLINOLIPID is contraindicated in pre-term infants, and in individuals allergic to egg and soybean. The product should not be given to children, as it is unknown if it would provide adequate amounts of essential fatty acids.²⁰⁷ To date, this product has not appeared on the market and stability studies in parenteral nutrition solutions have not been performed.

Liraglutide (SAXENDA, approved 12/23/14), a GLP-1 receptor antagonist was previously approved for the treatment of type 2 diabetes as VICTOZA. SAXENDA brand liraglutide is indicated for weight management in obese adults and overweight adults with hypertension, type 2 diabetes, or high cholesterol. The initial dosage regimen for weight management is 0.6 mg by subcutaneous injection daily. The dose can be increased by 0.6 mg weekly up to a maximum of 3 mg daily to minimize gastrointestinal side effects. If the patient has not lost at least 4% of their body weight by week 16, the drug should be discontinued. The two brands of liraglutide should not be interchanged. Prescribing information includes a black box warning about thyroid cancer.²⁰⁸ Liraglutide was approved with a REMS communication plan that informs prescribers of the product's risks.⁶⁶ See **Table 16**.

Imaging Contrast and Radiology Drugs

Since health-system pharmacies are increasingly involved in the procurement of agents used in radiology and nuclear medicine, the following products are included for purposes of completeness.

Sulfur hexafluoride lipid microsphere (LUMASON, approved 10/10/14) is a contrast medium used to enhance ultrasound waves in echocardiograms and assist in viewing the image of the heart. It is administered by intravenous bolus injection during echocardiography.^{209,210}

Gadoterate meglumine (DOTAREM, approved 3/20/13) is a contrast medium that allows for better viewing of central nervous system images during magnetic reso-

nance imaging (MRI). The product is administered by intravenous bolus injection.^{211,212}

Technetium 99m tilmanocept (LYMPHOSEEK, approved 3/13/13) is a radioactive diagnostic imaging agent used to map lymph nodes near tumors to assist in their surgical removal. This diagnostic is administered by intradermal, subcutaneous, or peritumoral (around a tumor) injection. This product is stored within a radiation shield and should only be used by those licensed to handle radiopharmaceuticals.^{213,214}

Flutemetamol F-18 (VIZAMYL, approved 10/25/13) and florbetaben F-18 (NUERACEQ, approved 10/25/2013) are radioactive diagnostic drugs for use in positron emission tomography (PET) of the brain in patients with dementia and Alzheimer's disease. They are used to estimate the density of amyloid neuritic plaques. These diagnostics are administered by intravenous bolus injection. These products are stored within a radiation shield and should only be used by those licensed to handle radiopharmaceuticals.^{215,216,217}

Radium 223 dichloride (XOFIGO, approved 5/15/13) is a radioactive drug for the treatment of castration-resistant prostate cancer. It is administered by slow intravenous injection every 4 weeks for 6 injections. This product is stored within a radiation shield and should only be used by those licensed to handle radiopharmaceuticals.^{218,219,220} See **Table 17**.

CONCLUSION

After this review, it becomes obvious that our understanding of disease is growing exponentially each year as molecular causes of disease are discovered and drugs are developed to combat increasingly complex disease states. With over 40 new drugs approved in 2013 and over 50 approved in 2014, the pharmacy technician is challenged to keep up with new information related to obtaining and handling these new products in the pharmacy.

Table 16. New Miscellaneous Drugs

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Lipid injectable emulsion (CLINOLIPID) ^a <i>Approved 10/3/13</i>	Emulsion for intravenous infusion	0338-9540-04 0338-9540-08	20% 1000 mL (1) 20% 1000 mL (6)	Store at room temperature. Do not freeze, Avoid excessive heat. Store in overpouch (contains oxygen absorber/sensor) until use
Liraglutide (SAXENDA) ^b <i>Approved 12/23/14</i>	Solution for subcutaneous injection	0169-2800-13 0169-2800-15	6 mg/mL (3 mL) prefilled multi-dose pen (3) 6 mg/mL (3 mL) prefilled multi-dose pen (5) Each pen delivers 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg doses	Refrigerate. Do not freeze. After initial use, may be stored at room temperature for 30 days. Protect from heat. Protect from sunlight.

^a CLINOLIPID (lipid injectable emulsion) [package insert]. Baxter Healthcare Corporation; October 2013

^b SAXENDA (generic) [package insert]. Novo Nordisk, Inc.; March 2015.

Table 17. New Drugs for Imaging, Contrast and Radiology

Generic Name (BRAND NAME)	Dosage Form	NDC	Product Description (Quantity)	Storage Conditions
Flutemetamol F18 (VIZAMYL) ^a <i>Approved 10/25/13</i>	Solution for injection	17156-067-10 17156-067-30	10 mL 150 MBq/mL multi-dose vial 30 mL 150 MBq/mL multi-dose vial	Store at room temperature. Store within radiation shielding. Do not dilute. For use only by persons licensed by the Nuclear Regulatory Commission.
Gadoterate meglumine (DOTAREM) ^b <i>Approved 3/20/13</i>	Solution for injection	67684-200-01 67684-200-02 67684-200-03 67584-300-01 67684-300-02 67684-300-03	10 mL 0.5 mmol/mL vial (10) 15 mL 0.5 mmol/mL vial (10) 20 mL 0.5 mmol/mL vial (10) 10 mL 0.5 mmol/mL pre-filled syringe (5) 15 mL 0.5 mmol/mL pre-filled syringe (5) 20 mL 0.5 mmol/mL pre-filled syringe (5)	Store at room temperature. Do not freeze syringes, discard if frozen.
Florbetaben F18 (NUERACEQ) ^c <i>Approved 3/19/14</i>	Solution for injection	54828-001-30	30 mL 50 -5000 MBq/mL multi-dose vial	Store at room temperature Store in original container or equivalent radiation shielding. Do not dilute. For use only by persons licensed by the Nuclear Regulatory Commission.
Radium 233 dichloride (XOFIGO) ^d <i>Approved 5/15/13</i>	Solution for injection	50419-208-01	6 mL 1,000 kBq/mL single-use vial	Store at room temperature Store in original container or equivalent radiation shielding. For use only by persons licensed by the Nuclear Regulatory Commission.
Sulfur hexafluoride lipid microspheres (LUMASON) ^e <i>Approved 10/10/14</i>	Lyophilized powder for injection	0270-7099-15	Supplied 5 kits/carton, each kit contains: 25 mg lipid-type A vial (1) 5 mL normal saline prefilled syringe (1) Mini-spike (1)	Store at room temperature. Use within 3 hours of reconstitution.
Technetium 99m tilmanocept (LYMPHOSEEK) ^f <i>Approved 3/13/13</i>	Injection	52579-1695-1 52579-1640-1	250 mcg powder vials (5) 4.5 mL buffered saline diluent vials (5) Labels for shields (5) Labels for product vials and syringes (25)	Store at room temperature. Store in original container or equivalent radiation shielding. Use within 6 hours of preparation For use only by persons licensed by the Nuclear Regulatory Commission.

^a VIZAMYL (flutemetamol F18) [package insert]. GE Healthcare; December 2014

^b DOTAREM (gadoterate meglumine) [package insert]. Guerbet LLC; March 2013

^c NUERACEQ (florbetaben F18) [package insert]. Piramal Imaging; March 2013

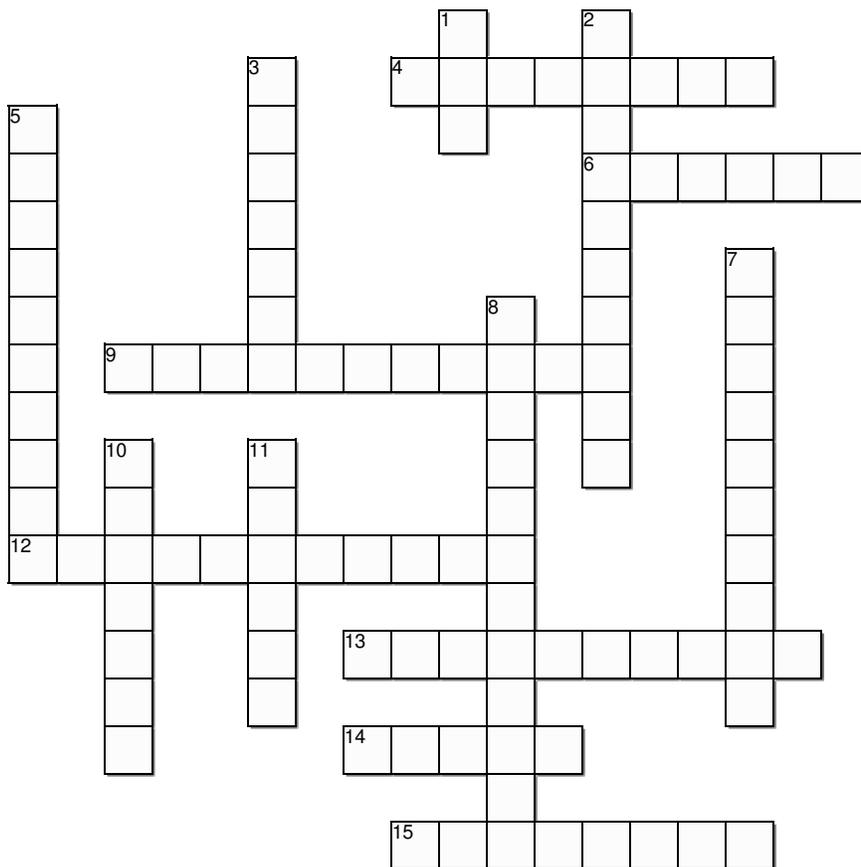
^d XOFIGO (radium 233 dichloride) [package insert]. Bayer HealthCare Pharmaceuticals, Inc.; May 2013

^e LUMASON (sulfur hexafluoride lipid-type A microspheres) [package insert]. Bracco Diagnostics, Inc.; October 2014

^f LYMPHOSEEK (technetium Tc 99m tilmanocept) [package insert]. Navidea Biopharmaceuticals, Inc.; October 2014

New Drugs Crossword Puzzle D

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

4. OBIZUR is used for adults with _____ hemophilia A.
6. Tedizolid (SIVEXTRO) is given intravenously or _____.
9. Route of administration for peramivir (RAPIVAB).
12. The generic name for SAXENDA and VICTOZA.
13. TOBI PODHALER is used to deliver _____ into the lungs of patients with cystic fibrosis.
14. CLINOLIPID lipid emulsion injection is made from soybean and _____ oil.
15. KCENTRA is used for the reversal of _____ anticoagulation.

Down

1. VIEKIRA PAK is a 4-drug combination product for _____.
2. Generic name for KYNAMRO.
3. Eliglustat (CERDELGA) is an oral treatment for _____ disease.
5. ELOCTATE is used for adults and children with _____ hemophilia A.
7. Dalbavancin (DALVANCE) and oritavancin (ORBACTIV) are in the same drug category as _____.
8. The generic name for HIV drug TIVICAY.
10. Take great care when interpreting this drug's dose at the time of compounding.
11. Dalbavancin (DALVANCE) and oritavancin (ORBACTIV) are INCOMPATIBLE with _____.

Answers on page 54.

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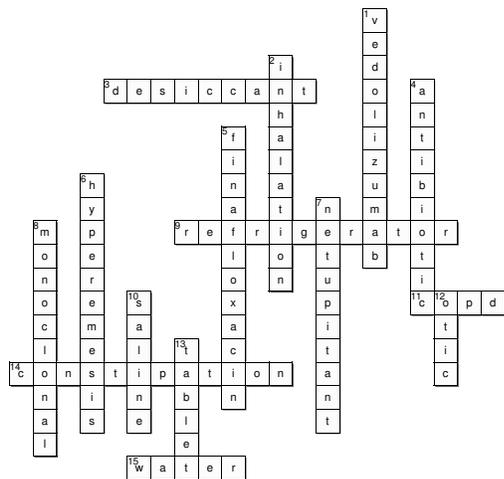
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166. FDA approves Opsumit to treat pulmonary arterial hypertension. FDA News Release; October 18, 2013.
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198. FDA approves the first antihemophilic factor, Fc fusion protein for patients with Hemophilia A. FDA News Release; June 6, 2014.
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205. Siltuximab (Sylvant) for Treatment of Multicentric Castleman's Disease. The Medical Letter; January 15, 2015.
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207. FDA approves Clinolipid for intravenous nutrition. FDA News Release; October 3, 2013.
208. FDA approves weight-management drug Saxenda. FDA News Release; December 23, 2014.
209. FDA approves a new ultrasound imaging agent. FDA News Release; October 10, 2014.
210. LUMASON (sulfur hexafluoride lipid-type A microspheres) [package insert]. Bracco Diagnostics, Inc.; October 2014
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212. DOTAREM (gadoterate meglumine) [package insert]. Guerbet LLC; March 2013
213. FDA approves Lymphoseek to help locate lymph nodes in patients with certain cancers. FDA News Release; March 13, 2013.
214. LYMPHOSEEK (technetium Tc 99m tilmanocept) [package insert]. Navidea Biopharmaceuticals, Inc.; October 2014
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216. VIZAMYL (flutemetamol F18) [package insert]. GE Healthcare; December 2014
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ANSWER KEY:

New Drugs Crossword Puzzle A

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

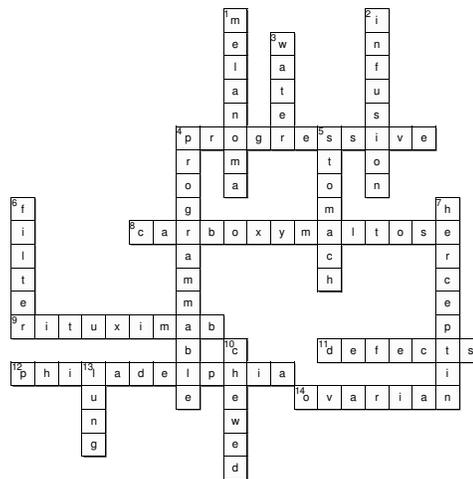
- 3. Item that should not be removed from DICLEGIS' original packaging. (**desiccant**)
- 9. ENTYVIO should be stored in the _____. (**refrigerator**)
- 11. BREO ELLIPTA and ANORO ELLIPTA indication. (**copd**)
- 14. MOVANTIK is indicated for opioid-induced _____. (**constipation**)
- 15. Sterile _____ is used to reconstitute ENTYVIO. (**water**)

Down

- 1. The generic name for ENTYVIO. (**vedolizumab**)
- 2. The route of administration for BREO ELLIPTA and ANORO ELLIPTA. (**inhalation**)
- 4. XTORO belongs to which drug class? (**antibiotic**)
- 5. The generic name for XTORO. (**finlaxocin**)
- 6. DICLEGIS is indicated for _____. (**hyperemesis**)
- 7. _____ and palonosetron (AKYZEO) is indicated in chemotherapy-induced nausea and vomiting. (**netupitant**)
- 8. ENTYVIO is a(n) _____ antibody. (**monoclonal**)
- 10. Once reconstituted, _____ is used to dilute ENTYVIO. (**saline**)
- 12. The route of administration for XTORO. (**otic**)
- 13. MOVANTIK dosage form. (**tablet**)

New Drugs Crossword Puzzle C

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

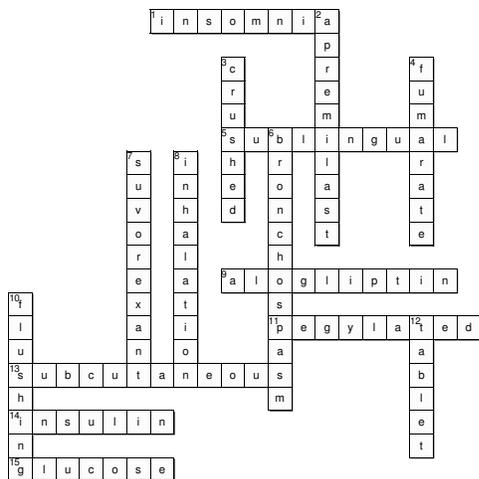
- 4. Obinutuzumab (GAZYVA) has a black box warning for _____. (**multifocal leukoencephalopathy**)
- 8. The newest parenteral iron product is ferric _____. (**INJECTAFER**). (**carboxymaltose**)
- 9. Idelalisib is used in combination with _____. (**RITUXAN**). (**rituximab**)
- 11. Pomalidomide (POMALYST) can cause birth _____. (**defects**)
- 12. Blinatumomab (BLINCYTO) is indicated in _____ chromosome-negative acute lymphoblastic leukemia. (**philadelphia**)
- 14. Olaparib (LYNPARZA) is approved for _____ cancer. (**ovarian**)

Down

- 1. Dabrafenib (TAFINLAR), trametinib (MEKINIST), pembrolizumab (KEYTRUDA), and nivolumab (OPDIVO) are approved for use in late-stage _____. (**melanoma**)
- 2. INJECTAFER is administered by intravenous _____ or intravenous "push" injection. (**infusion**)
- 3. Ibrutinib (IMBRUVICA) is administered with a glass of _____. (**water**)
- 4. Blinatumomab (BLINCYTO) must be administered through a(n) _____ electronic ambulatory infusion pump. (**programmable**)
- 5. Ramucicromab (CYRAMZA) is approved for _____ cancer. (**stomach**)
- 6. Ado-trastuzumab (KADCYLA) is administered through a 0.22 micron _____. (**filter**)
- 7. Ado-trastuzumab (KADCYLA) should NOT be confused with trastuzumab _____. (**herceptin**)
- 10. Ibrutinib (IMBRUVICA) tablets should not be crushed or _____. (**chewed**)
- 13. Afatinib (GILOTRIF) and ceritinib (ZYPADIA) are approved for _____ cancer. (**lung**)

New Drugs Crossword Puzzle B

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

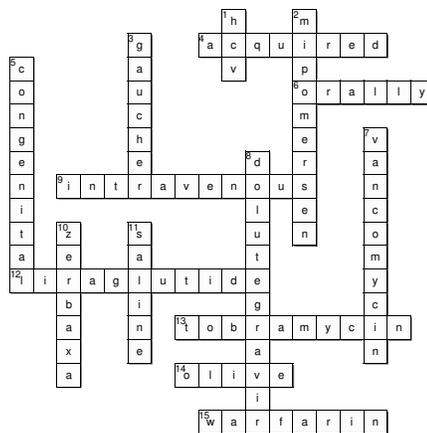
- 1. BELSOMRA indication. (**insomnia**)
- 5. Route of administration for ORALAIR, RAGWITEK, and GRASTEK. (**sublingual**)
- 9. The "gliptin" component of KAZANO and OSENI. (**alogliptin**)
- 11. Peginterferon beta-1a (PLEGRIDY) is a _____ form of interferon beta-1a. (**pegylated**)
- 13. Route of administration for PLEGRIDY. (**subcutaneous**)
- 14. GLP-1 receptor agonists decrease blood sugar by increasing _____. (**insulin**)
- 15. SGLT2 inhibitors decrease blood sugar by increasing kidney excretion of _____. (**glucose**)

Down

- 2. The generic name for OTEZLA. (**apremilast**)
- 3. Levomilnacipran (FETZIMA) capsules should not be _____. (**crushed**)
- 4. The generic name for TECFIDERA is dimethyl _____. (**fumarate**)
- 6. AFREZZA brand human insulin has a black box warning for _____. (**bronchospasm**)
- 7. The generic name for BELSOMRA. (**suvorexant**)
- 8. Route of administration of AFREZZA brand human insulin. (**inhalation**)
- 10. _____ decreases when TECFIDERA is taken with food. (**flushing**)
- 12. Vortioxetine (BRINTELLIX) dosage form. (**tablet**)

New Drugs Crossword Puzzle D

Complete the crossword by answering the clues provided.



Created on TheTeachersCorner.net Crossword Maker

Across

- 4. OBIZUR is used for adults with _____ hemophilia A. (**acquired**)
- 6. Tedizolid (SIVEXTRO) is given intravenously or _____. (**orally**)
- 9. Route of administration for peramivir (RAPIVAB). (**intravenous**)
- 12. The generic name for SAXENDA and VICTOZA. (**liraglutide**)
- 13. TOBI PODHALER is used to deliver _____ into the lungs of patients with cystic fibrosis. (**tobramycin**)
- 14. CLINOLIPID lipid emulsion injection is made from soybean and _____ oil. (**olive**)
- 15. KCENTRA is used for the reversal of _____ anticoagulation. (**warfarin**)

Down

- 1. VIEKIRA PAK is a 4-drug combination product for _____. (**hep**)
- 2. Generic name for KYNAMRO. (**mipomersen**)
- 3. Eliglustat (CERDELGA) is an oral treatment for _____ disease. (**gaucher**)
- 5. ELOCTATE is used for adults and children with _____ hemophilia A. (**congenital**)
- 7. Dalbavancin (DALVANCE) and oritavancin (ORBACTIV) are in the same drug category as _____. (**vancomycin**)
- 8. The generic name for HIV drug TIVICAY. (**dolutegravir**)
- 10. Take great care when interpreting this drug's sdate at the time of compounding. (**zerbaxa**)
- 11. Dalbavancin (DALVANCE) and oritavancin (ORBACTIV) are INCOMPATIBLE with _____. (**saline**)

ANSWER KEY:

Created with TheTeachersCorner.net Word Search Maker

Orphan Drug Search

Can you find 30 orphan generic or brand drug names?

N	G	Q	O	B	I	Z	U	R	A	R	T	N	E	C	K	I	N	K	T
E	Y	S	Y	A	F	V	C	A	R	E	H	T	R	O	N	J	I	K	A
T	S	A	T	M	N	I	T	P	E	L	E	R	T	E	M	L	B	F	T
T	N	P	I	I	Y	Z	X	I	X	K	S	Y	L	V	A	N	T	N	S
E	D	M	M	X	A	A	R	R	L	W	H	W	E	G	S	E	I	M	U
R	A	E	U	U	V	L	I	F	N	L	L	R	Q	I	Y	N	I	S	L
T	G	D	S	T	U	P	O	E	L	A	J	F	B	L	T	P	E	V	G
L	L	A	P	L	F	R	C	N	B	V	T	U	C	E	O	O	T	I	I
P	E	E	O	I	X	O	I	I	B	Q	X	N	D	M	I	P	O	M	L
C	D	T	S	S	K	L	G	D	D	I	R	A	E	Z	B	H	B	I	E
U	R	E	X	B	G	I	U	O	R	J	N	R	L	T	I	Z	I	Z	L
Z	E	K	X	D	R	X	A	N	O	I	S	I	O	P	I	O	H	I	B
U	C	M	A	L	B	I	T	E	B	E	V	A	S	E	H	C	D	M	E
E	T	A	T	C	O	L	E	W	N	Y	E	C	U	L	E	P	A	Y	R
R	B	Y	Z	Z	I	C	T	G	V	F	G	L	A	T	M	Q	M	I	
A	P	O	D	I	X	O	R	D	L	W	O	T	F	Y	L	A	T	R	G
Z	M	X	D	O	R	M	A	N	Y	K	X	Y	A	M	I	B	R	V	J
M	T	T	J	R	U	C	O	N	E	S	T	F	S	H	O	P	K	X	M
X	A	U	J	O	C	Y	P	A	K	S	O	G	E	J	Z	G	Z	V	S
V	O	W	T	N	O	E	T	L	E	M	I	S	A	T	J	U	C	K	F

ADEMPAS	KYNAMRO	PIRFENIDONE
ALPROLIX	MACITENTAN	RIOCIGUAT
CERDELGA	METRELEPTIN	RIXUBIS
DROXIDOPA	MIPOMERSEN	RUCONEST
ELIGLUSTAT	MYALEPT	SILTUXIMAB
ELOCTATE	NINTEDANIB	SYLVANT
ELOSULFASE	NORTHERA	TASIMELTEON
ESBRIET	OBIZUR	TOBI
HETLIOZ	OFEV	TRETTEN
KCENTRA	OPSUMIT	VIMIZIM

SELF ASSESSMENT QUESTIONS

1. Which of the following is TRUE about the ear drop finafloxacin (XTORO)?
 - A. It should be stored in the freezer.
 - B. It should be stored in the refrigerator.
 - C. The patient should warm the bottle in their hands for two minutes prior to administration.
 - D. The dose is one drop into the affected ear three times daily.

2. When preparing the antiplatelet drug vorapaxar (ZONTIVITY) for dispensing, _____.
 - A. place it in an amber plastic bottle.
 - B. dispense it in its original container with the desiccant in place.
 - C. place it in a weekly pill box to help in patient adherence.
 - D. keep it refrigerated until pick-up.

3. The bronchodilator vilanterol is available in combination with the corticosteroid fluticasone (BREO ELLIPTA) and the anticholinergic umeclidinium (ANORO ELLIPTA). It is indicated in the treatment of _____.
 - A. cystic fibrosis.
 - B. idiopathic pulmonary fibrosis.
 - C. pulmonary arterial hypertension.
 - D. chronic obstructive pulmonary disease.

4. The beyond-use dating of reconstituted and diluted vedolizumab (ENTYVIO) is _____.
 - A. 4 hours
 - B. 24 hours
 - C. 2 weeks
 - D. 8 weeks

5. Which of the following is TRUE about the components of DICLEGIS?
 - A. The previous formulation, BENDECTIN, caused birth defects.
 - B. Doxylamine causes insomnia.
 - C. Pyridoxine is another name for vitamin C.
 - D. The combination is used in the treatment of severe nausea and vomiting during pregnancy.

6. The “sleeping pill” suvorexant (BELSOMRA) _____.
 - A. may cause a patient to unknowingly perform activities when not awake.
 - B. is a Schedule-II controlled substance.
 - C. may be taken with grapefruit juice.
 - D. can be taken 4 hours before planned awakening.

7. Eslicarbazepine (APTIOM) _____.
 - A. is used in the treatment of insomnia.
 - B. should be discontinued quickly.
 - C. requires higher dosing in kidney failure.
 - D. could cause suicidal thoughts.

8. In 2013 and 2014, two drugs were approved for multiple sclerosis. They are:
 - A. Dimethyl fumarate (TECFIDERA) and peginterferon-2b (PEGINTRON)
 - B. Fingolimod (GILENYA) and peginterferon alfa-2a (PEGASYS)
 - C. Dimethyl fumarate (TECFIDERA) and peginterferon beta-1a (PLEGRIDY)
 - D. Teriflunomide (AUBAGIO) and interferon beta-1a (AVONEX)

9. Antidepressants levomilnacipran (FETZIMA) and vortioxetine (BRINTELLIX) have a black box warning for _____.
 - A. thyroid tumors.
 - B. suicidal thoughts.
 - C. heart failure.
 - D. asthma.

10. Which of the following is true about the antiarthritic apremilast (OTEZLA)?
 - A. The tablet should not be crushed, chewed, or split.
 - B. It is available as a subcutaneous injection.
 - C. It must be taken on an empty stomach.
 - D. Patients with kidney problems should take double doses.

11. **ORALAIR, GRASTEK, and RAGWITEK** _____.
A. contain ragweed extracts.
B. are administered sublingually in children and adults.
C. are administered by injection in an allergist's office.
D. are beneficial in patients with asthma.
12. **Albiglutide (TANZEUM) and dulaglutide (TRULICITY)** _____.
A. are given orally.
B. are used in type 2 diabetes.
C. are used in place of diet and exercise.
D. decrease insulin and increase glucagon.
13. **Which of the following is TRUE about ferric carboxymaltose (INJECTAFER)?**
A. It is administered by subcutaneous injection.
B. Severe allergic reactions occur more often than with iron dextran (INFED).
C. It is administered daily until iron stores normalize.
D. It can leave a dark brown discoloration if it extravasates.
14. **Blinatumomab (BLINCYTO) is a novel bi-specific T-cell engager. This means that** _____.
A. it is a chemotherapeutic agent fused with a monoclonal antibody.
B. it is a cancer-specific laboratory test.
C. it is given for two doses only.
D. it is fused from two different antibodies to bring T-cells to affected B-cells.
15. **To prevent infusion-related reactions to obinutuzumab (GAZYVA), patients may be pre-medicated with** _____.
A. a glucocorticoid.
B. acetaminophen.
C. an antihistamine
D. all of the above.
16. **Pomalidomide (POMALYST) has a REMS program because it can cause** _____.
A. kidney failure.
B. fetal damage.
C. heart failure.
D. lung infections.
17. **Chemotherapy precautions must be used in the handling, preparation, and administration of** _____.
A. belinostat (BELEODAQ) and Ado-trastuzumab (KADCYLA)
B. blinatumomab (BLINCYTO) and obinutuzumab (GAZYVA)
C. pomalidomide (POMALYST) and pembrolizumab (KEYTRUDA)
D. ceritinib (ZYKADIA) and ramucirumab (CYRAMZA)
18. **Ramucirumab (CYRAMZA) and ado-trastuzumab (KADCYLA) must be diluted into** _____.
A. dextrose
B. water
C. Lactated Ringers
D. normal saline
19. **Oritavancin (ORBACTIV) is administered intravenously** _____.
A. monthly.
B. weekly.
C. daily.
D. once.
20. **When reconstituting metreleptin (MYALEPT) for use in infants, use** _____.
A. sterile water without bacteriostat.
B. bacteriostatic water.
C. sterile saline without bacteriostat.
D. bacteriostatic saline.