



PHARMACY PRÉCIS



Précis: a concise summary of essential points, statements or facts

Volume 31 (Issue 1)

January 2013

New Molecular Entities of July to December 2012

New [molecular entities](#), [biologic agents](#), [drug formulations/combinations](#), and [drug indications](#) approved during 2012 (including indication, approval date, and comments) are presented in this issue of *Pharmacy Précis*. An explanation of the FDA classification of the new drugs also is included. If you need any additional information regarding these agents, please call the Samford University Global Drug Information Service at (205) 726-2659.

FDA classification for newly approved drugs is based on chemical classification and is outlined below.

FDA CLASSIFICATIONS		
CHEMICAL CLASSIFICATION	THERAPEUTIC CLASSIFICATION	ADDITIONAL CLASSIFICATION
<ol style="list-style-type: none"> New molecular entity - drug not marketed in U.S. by any manufacturer New salt - active moiety is marketed in the U.S., but this particular salt, ester, or derivative is not New formulation - drug marketed in the U.S., but this particular formulation is not New combination - two or more ingredients in combination not marketed in the U.S. New manufacturer - already marketed by another firm; duplicated salt, formulation or combination New indication - already marketed by same firm but used primarily for new indications Marketed without an approved NDA OTC Switch 	<p>S = Standard review - assigned to drugs that appear to have therapeutic qualities similar to drugs already approved</p> <p>P = Priority review - assigned to drugs that appear to have therapeutic gain over drugs currently available</p> <p>O = Orphan designation - Pursuant to Section 526 of the Orphan Drug Act (Public Law 97-414 as amended).</p> <ol style="list-style-type: none"> Providing effective therapy or diagnosis for a disease not adequately treated or diagnosed by any marketed drug Providing improved treatment or greater effectiveness or safety Having a modest, but real advantage over convenience, elimination of troublesome side-effects, or treatment of a specific sub-population of patients 	<p>AA = AIDS drugs (always classified as P)</p> <p>E = Drugs that treat life-threatening or severely debilitating diseases</p> <p>F = Possible fraudulently submitted data</p> <p>G = Data from a type F classification is validated</p> <p>N = Nonprescription drug</p> <p>V = Designated orphan drug</p>

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Samford University Global Drug Information Service

NEW MOLECULAR ENTITIES OF 2012

(Click on generic drug name for further information)

GENERIC NAME (BRAND NAME)	SPONSOR	CATEGORY	APPROVAL DATE
Sodium Picosulfate; Magnesium Oxide; Citric Acid (Prepopik)	Ferring Pharmaceuticals Inc	1S	July 16, 2012
Carfilzomib (Kyprolis)	Onyx Pharmaceuticals Inc.	1S	July 20, 2012
Acidinium Bromide (Tudorza Pressair)	Forest Labs Inc.	1S	July 23, 2012
Icosapent Ethyl (Vascepa)	Amarin Pharma Inc.	S	July 26, 2012
Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate (Stribild)	Gilead Sciences, Inc.	1S	Aug 27, 2012
Linaclotide (Linzess)	Forest Laboratories	1S	Aug 30, 2012
Enzalutamide (Xtandi)	Medivation	1P	Aug 31, 2012
Bosutinib (Bosulif)	Wyeth Pharms	1S	Sept 4, 2012
Teriflunomide (Aubagio)	Sanofi Aventis	1S	Sept 12, 2012
Choline C-11	Mayo Clinic PET Radiochemistry Facility	1P	Sept 12, 2012
Poly-Ureurethane (Nuvail)	Innocutis Holdings	–	Sept 18, 2012
Regorafenib (Stivarga)	Bayer Healthcare	1P	Sept 27, 2012
Perampanel (Fycompa)	Eisai Inc.	1S	Oct 22, 2012
Omacetaxine Mepesuccinate (Synribo)	Ivax Pharms	1S	Oct 26, 2012
Tofacitinib (Xeljanz)	Pfizer Inc.	1S	Nov 06, 2012
Cabozantinib (Cometriq)	Exelixis Inc.	1P	Nov 29, 2012
Pasireotide Diaspartate (Signifor)	Novartis	1S	Dec 14, 2012
Ponatinib (Iclusig)	Ariad	1P	Dec 14, 2012
Teduglutide (Gattex)	Nps Pharms Inc.	1S	Dec 21, 2012
Lomitapide (Juxtapid)	Aegerion	1S	Dec 21, 2012
Apixaban (Eliquis)	Bristol Myers Squibb	1P	Dec 28, 2012
Bedaquiline (Sirturo)	Janssen Therap	1P	Dec 28, 2012
Crofelemer (Fulyzaq)	Salix Pharms	1P	Dec 31, 2012

Sodium Picosulfate; Magnesium Oxide; Citric Acid (Prepopik, Ferring Pharmaceuticals Inc)

Pharmacology: Osmotic Laxative; Laxative Stimulant.

Indication: Indicated for bowel cleansing prior to colonoscopy in adults.

Adverse Drug Reactions: Most commonly reported adverse reactions, occurring $\geq 1\%$, are nausea, headache and vomiting.

Dose: Reconstitute right before each administration by filling the supplied dosing cup with 5-ounces of cold water and pour the contents of one packet of powder and stir for two to three minutes. The manufacturer recommends the "Split-Dose" regimen, which consist of instructing the patient to take two separate doses in conjunction with fluids, as follows: take the first dose during the evening before the colonoscopy (i.e., 5:00 to 9:00 PM) followed by five 8-ounce drinks of clear liquids before bed. Consume clear liquids within 5 hours. Take second dose, the next day approximately 5 hours before the colonoscopy followed by at least three 8-ounce drinks of clear liquids before the colonoscopy. Consume clear liquids within 5 hours up until 2 hours before the time of the colonoscopy. If splitting the dose is inappropriate for the patient the manufacturer offers an "alternate" dosing regimen. Administer the first dose in the afternoon or early evening (i.e., 4:00 to 6:00 PM) before the colonoscopy followed by five 8-ounce drinks of clear liquids within 5 hours. The second dose should be administered approximately 6 hours later in the evening (i.e., 10:00 PM to 12:00 AM) followed by 24-ounces of clear liquids within 5 hours.

Formulation: Supplied as two packets of powder for reconstitution, each of which contain 10 mg sodium picosulfate, 3.5 g magnesium oxide, and 12 g anhydrous citric acid in 16.1 grams of powder.

[\(Back to New Molecular Entities Table\)](#)

Sodium Picosulfate; Magnesium Oxide; Citric Acid (Prepopik, Ferring Pharmaceuticals Inc)
(continued)

Warnings/Contraindications: Contraindications for therapy include: Severe renal dysfunction (CrCl < 30mL/min), gastrointestinal obstruction or ileus, bowel perforation, toxic colitis or toxic megacolon, gastric retention or an allergy to any of the listed ingredients. Serious fluid and serum chemistry abnormalities are possible, if a patient develops significant vomiting or signs of dehydration or orthostasis consider performing post-colonoscopy lab test (electrolytes, creatinine, and BUN) and treat accordingly. Osmotic laxatives may produce colonic mucosal aphthous ulcerations and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Patients with impaired gag reflex and patients prone to regurgitation or aspiration should be observed during administration. Generalized tonic-clonic seizure associated with and without hyponatremia in epileptic patients has been reported in post-marketing surveillance. Use caution in patients with conditions or who are using medications that increase the risk for fluid and electrolyte disturbances or may increase the risk of seizure, arrhythmias, and prolonged QT in the setting of fluid and electrolyte abnormalities.

Place in Therapy: The colon cleansing efficacy of sodium picosulfate, magnesium oxide, and citric acid was demonstrated in two randomized, single-blind, active-controlled trials (n=1195), in which the use of sodium picosulfate, magnesium oxide, and citric acid was non-inferior to polyethylene glycol plus electrolytes and bisacodyl.

Notes: Instruct patients to consume only clear liquids on the day before the colonoscopy up until two hours before the time of the colonoscopy. The second dose should be delayed until their symptoms resolve if patients experience severe bloating, distention, or abdominal pain following the first dose. Oral medication taken within 1 hour of start of each dosing may not be properly absorbed. Use caution in patients on concurrent NSAID or drugs known to induce SIADH (eg, tricyclic antidepressants, selective serotonin reuptake inhibitors, antipsychotic drugs and carbamazepine), as the risk of water retention and/or electrolyte imbalance may be increased.

Carfilzomib (Kyprolis, Onyx Pharmaceuticals, Inc.)

Pharmacology: Antineoplastic Agent; Proteasome Inhibitor.

Indication: Indicated for the treatment of patient with multiple myeloma who have received at least two prior therapies including; bortezomib and an immunomodulatory agent and demonstrated disease progression on or within 60 days of completion of the last therapy.

Adverse Drug Reactions: Most commonly occurring adverse reactions are fatigue, anemia, nausea, thrombocytopenia, dyspnea, diarrhea, and pyrexia. Serious events include pneumonia, acute renal failure, congestive heart failure, and death.

Dose: Administer intravenously over two to ten minutes, on two consecutive days each week for three weeks, followed by a twelve-day rest period. The recommended Cycle 1 dose is 20-mg/m²/day, and if tolerated increase Cycle 2 dose and subsequent cycles to 27-mg/m²/day. Modify dose based on toxicity. Premedicate with dexamethasone prior to all Cycle 1 doses, during the first cycle of dose escalation, and if infusion reaction symptoms develop or reappear. Patient should be hydrated prior to administration to avoid tumor lysis syndrome.

Formulation: 60-mg sterile lyophilized powder as a single-use vial.

Warnings/Contraindications: No contraindications listed by the manufacturer. Dose adjustments are needed for various toxicities including neutropenia, thrombocytopenia, cardiac, renal, or hepatic toxicity, pulmonary hypertension or complications, peripheral neuropathy, or other non-hematologic toxicities. Safety in patients with New York Heart Association (NYHA) class 3 or 4 heart failure has not been evaluated. New onset or worsening of pre-existing congestive heart failure with decreased left ventricular function or myocardial ischemia has occurred in 7% of patients following administration. Carfilzomib has been associated with hepatic failure, sometimes resulting in death, as well as, elevations of serum transaminases and bilirubin.

Place in Therapy: A safety and efficacy trial in 266 patients with relapsed multiple myeloma who had previously received at least two prior therapies and only showed ≤ 25% response or experienced disease progression during or within 60 days of the most recent therapy were enrolled. The primary endpoint, overall response rate (ORR), was [22.9% (95% CI: 18, 28.5) (n = 266)]. Median duration of response (DOR) in months, was [7.8% (95% CI: 5.6, 9.2) (n = 266)].

[\(Back to New Molecular Entities Table\)](#)

Carfilzomib (Kyprolis, Onyx Pharmaceuticals, Inc.) (continued)

Notes: Monitor platelet counts, liver enzymes, evidence of cardiac complications, tumor lysis syndrome, and dyspnea during treatment. Unopened vials should be stored refrigerated and protected from light.

Acclidinium Bromide (Tudorza Pressair, Forest Labs)

Pharmacology: Long-Acting Anticholinergic Agent.

Indication: Acclidinium bromide powder for inhalation is indicated for the long-term, maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

Adverse Drug Reactions: Most commonly occurring adverse effects are headache, nasopharyngitis and cough.

Dose: The recommended adult dose is one oral inhalation (400 mcg) twice daily.

Formulation: Available as a multi-dose dry powder for inhalation.

Warnings/Contraindications: Paradoxical bronchospasm, worsening of narrow-angle glaucoma and urinary retention have been noted with acclidinium bromide. Use cautiously in patients with narrow-angle glaucoma, prostatic hyperplasia, and bladder-neck obstruction. Serious events included 1st-degree atrioventricular block, cardiac failure, and cardiorespiratory arrest have been reported with acclidinium bromide.

Place in Therapy: Three randomized, double-blind, placebo-controlled trials in patients with COPD were conducted. Patients were randomized to receive acclidinium bromide 400-mcg twice daily or placebo. Results from these studies show that acclidinium bromide was associated with statistically significant improvements from baseline in morning pre-dose FEV₁ at 12 weeks compared to placebo.

Notes: Acclidinium bromide is not recommended for the initial treatment of acute bronchospasm episodes.

Icosapent Ethyl (Vascepa, Amarin Pharma Inc.)

Pharmacology: Eicosapentaenoic Acid (EPA).

Indication: Adjunct to diet to reduce triglyceride levels in adult patients with severe (≥ 500 -mg/dL) hypertriglyceridemia.

Adverse Drug Reactions: Most common adverse reaction reported was arthralgia.

Dose: Two grams twice daily with food.

Formulation: Available as a 1-gram capsule.

Warnings/Contraindications: Contraindicated in patients with a known hypersensitivity to fish oils. Patients with hepatic impairment should have transaminase levels monitored periodically during therapy.

Place in Therapy: The efficacy of icosapent ethyl was assessed in a randomized, placebo controlled, double-blind, parallel-group study of 151 adult patients with severe hypertriglyceridemia. Patients were randomized to receive 4 grams of icosapent ethyl or placebo for 12 weeks. Therapy with icosapent ethyl was associated with a 27% decrease from baseline of triglycerides, representing a 33% difference from baseline triglycerides compared to placebo [-33% (-47 to -22) p < 0.001].

Notes: The risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined. Omega-3 acids may prolong bleeding time. Patients receiving treatment with icosapent ethyl and other drugs affecting coagulation (e.g., anti-platelet agents) should be monitored periodically. Do not break open, crush, dissolve or chew capsule.

Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate (Stribild, Gilead Sciences, Inc.)

Pharmacology: Combination of 1 integrase strand transfer inhibitor, 1 pharmacokinetic enhancer, and 2 nucleos(t)ide analog HIV-1 reverse transcriptase inhibitors.

Indication: Treatment of HIV-1 infection in adults who are antiretroviral treatment-naïve.

Adverse Drug Reactions: Most common adverse drug reactions to Stribild were nausea and diarrhea.

Dose: One tablet taken once daily with food.

Formulation: Each tablet contains 150-mg of elvitegravir, 150-mg of cobicistat, 200-mg of emtricitabine, and 300- mg of tenofovir disoproxil fumarate.

Warnings/Contraindications: The concentration of drugs metabolized by CYP3A or CYP2D6 may be altered with concomitant Stribild administration. Drugs that induce CYP3A can alter the concentrations of one or more components of Stribild.

Elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate (Stribild, Gilead Sciences, Inc.)

Place in Therapy: Stribild contains two previously approved HIV drugs plus two new drugs, elvitegravir and cobicistat. The safety and efficacy was evaluated in 1,408 adult patients not previously treated for HIV in two double-blind clinical trials. Patients were randomly assigned to receive Stribild or Atripla (efavirenz/emtricitabine/ tenofovir disoproxil fumarate), an HIV drug that contains Truvada (emtricitabine and tenofovir disoproxil fumarate) and efavirenz, once daily in the first trial; and Stribild or Truvada plus atazanavir and ritonavir once daily in the second trial. The studies were designed to measure the percentage of patients who had an undetectable amount of HIV in their blood at 48 weeks. Results showed between 88 % and 90 % of patients treated with Stribild had an undetectable amount of HIV in their blood, compared with 84 % treated with Atripla and 87 percent treated with Truvada plus atazanavir and ritonavir.

Notes: Should not be initiated in patients with estimated creatinine clearance below 70 mL/min .
Discontinue in patients with estimated creatinine clearance below 50 mL /min.

Linacotide (Linzess, Forest Laboratories)

Pharmacology: Gastrointestinal Agent; Guanylate Cyclase-C Agonist.

Indication: Indicated for the treatment of Irritable bowel syndrome with constipation (IBS-C) and chronic idiopathic constipation (CIC).

Adverse Drug Reactions: Most commonly reported adverse events during clinical trial testing included diarrhea, abdominal pain, flatulence, and abdominal distension.

Dose: The recommended daily dose is 290 mcg and 145 mcg orally once daily for IBS-C and CIC, respectively.

Formulation: Available as 290-mcg and 145-mcg capsules.

Warnings/Contraindications: Contraindicated in pediatric patients up to 6 years of age and in patients with known or suspected mechanical gastrointestinal obstruction.

Place in Therapy: Linacotide was shown to be statistically better than placebo in two trials double-blind, placebo-controlled, randomized, multicenter trials with respect to the primary endpoint of the percentage of patients with and greater than 30% reduction in abdominal pain in a least 6 out of 12 weeks — trial 1: 12.7%; 95% CI, 5.8% to 19.5% and trial 2: 14.4%,95% CI, 7.6% to 21.1%. One of the main advantages of linacotide is the once daily dosing.

Notes: Linacotide should be held or discontinued if severe diarrhea occurs. Linacotide should be taken on an empty stomach at least 30 minutes prior to first meal of the day.

Enzalutamide (Xtandi, Medivation Inc)

Pharmacology: Androgen Receptor Inhibitor.

Indication: Indicated for the treatment of patients with metastatic castration-resistant prostate cancer who have previously received docetaxel.

Adverse Drug Reactions: Adverse reactions that occurred > 5% include: asthenia/fatigue, back pain, diarrhea, arthralgia, hot flush, peripheral edema, musculoskeletal pain, headache, upper respiratory infection, muscular weakness, dizziness, insomnia, lower respiratory infection, spinal cord compression and cauda equina syndrome, hematuria, paresthesia, anxiety, and hypertension.

Dose: The recommended dose is 160 mg (four 40 mg capsules) orally once daily.

Formulation: Available as a 40-mg capsule.

Warnings/Contraindications: Contraindicated in patients that are pregnant. Seizure occurred in 0.9% of patients receiving enzalutamide. There is no clinical trial experience with enzalutamide in patients who have had a seizure, in patients with predisposing factors for seizure, or in patients using concomitant medications that may lower the seizure threshold.

Place in Therapy: The efficacy and safety of enzalutamide in patients with metastatic castration-resistant prostate cancer who had received prior docetaxel-based therapy were assessed in a randomized, placebo-controlled, multicenter phase 3 clinical trial. The primary endpoint was overall survival. A total of 1199 patients were randomized 2:1 to receive either enzalutamide orally at a dose of 160 mg once daily (N = 800) or placebo orally once daily (N = 399). The median overall survival in patient taking enzalutamide was 18.4 months (n=800) compared to 13.6 months (n=399) in the placebo group, Hazard ratio = 0.63 95%; CI, 0.53 to 0.75 P <.0001.

Notes: May be taken with or without food.

Bosutinib (Bosulif, Pfizer Labs)

Pharmacology: Antineoplastic Agent, Tyrosine Kinase Inhibitor.

Indication: Treatment of adult patients with chronic, accelerated, or blast phase Philadelphia positive chronic myelogenous leukemia (Ph+ CML) with resistance or intolerance to prior therapy.

Adverse Drug Reactions: Most common adverse reactions include; diarrhea, nausea, thrombocytopenia, vomiting, abdominal pain, rash, anemia, pyrexia, and fatigue.

Dose: 500 mg orally once daily with food.

Formulation: 100-mg and 500-mg tablets.

Warnings/Contraindications: Gastrointestinal toxicity, myelosuppression, fluid retention and embryo fetal toxicity have been reported with bosutinib.

Bosutinib (Bosulif, Pfizer Labs) (continued)

Place in Therapy: Efficacy of bosutinib was shown in a multicenter, single-arm, open-label trial in 546 patients with Imatinib-Resistant or -Intolerant Ph+ Chronic Phase (CP), Accelerated Phase (AP) and Blast Phase (BP) CML. The primary efficacy endpoint for patients with CP CML previously treated with imatinib (n=266) or imatinib and dasatinib or nilotinib (n=108) was the rate of attaining a major cytogenetic response (MCyR) at week 24. Bosutinib resulted in a statistically significant response rate in both patient populations — 33.8% 95% CI, 28.2 to 39.9 and in patients previously treated with imatinib and 26.9% 95% CI, 18.8 to 36.2 in patients previously treated with imatinib and dasatinib or nilotinib. Patients with previously treated AP and BP CML also showed and statistically significant changes in the confirmed complete hematologic response (CHR) and overall hematologic response (OHR).

Notes: Females of reproductive potential should avoid becoming pregnant while being treated bosutinib.

Teriflunomide (Aubagio, Sanofi Aventis)

Pharmacology: Pyrimidine Synthesis Inhibitor.

Indication: Treatment of patients with relapsing forms of multiple sclerosis.

Adverse Drug Reactions: Most common adverse reactions include; ALT increased, alopecia, diarrhea, influenza, nausea, and paresthesia.

Dose: 7 mg or 14 mg orally once daily, with or without food.

Formulation: Available as 7 mg or 14 mg film-coated tablets.

Black box warnings/Contraindications: **Hepatotoxicity:** Severe liver injury including fatal liver failure has been reported in patients treated with leflunomide, which is indicated for rheumatoid arthritis. A similar risk would be expected for teriflunomide because recommended doses of teriflunomide and leflunomide result in a similar range of plasma concentrations of teriflunomide. If drug induced liver injury is suspected, discontinue teriflunomide and start accelerated elimination procedure.

Risk of Teratogenicity: Based on animal data, teriflunomide may cause major birth defects if used during pregnancy. Contraindicated in pregnant women or women of childbearing potential who are not using reliable contraception, pregnancy must be avoided during treatment.

Place in Therapy: In a 108 week, randomized double blind phase 3 trial the annual relapse rate of teriflunomide was reduced significantly (relative risk reduction, 31%) when compared with placebo in 1088 patients.

Notes: Obtain transaminase and bilirubin levels within 6 months before initiation, and monitor ALT levels at least monthly for six months.

Choline C-11 (Choline C-11, Mayo Clinic PET Radiochemistry Facility)

Pharmacology: Radiopharmaceutical.

Indication: Positron emission tomography (PET) imaging of patients with suspected prostate cancer recurrence and non-informative bone scintigraphy, computerized tomography (CT) or magnetic resonance imaging (MRI).

Adverse Drug Reactions: Mild injection site reaction, no other adverse reactions have been reported.

Dose: Administer 37 to 740 MBq (10 to 20 mCi) as an IV bolus injection. Initiate imaging immediately after administration and acquire static emission images 0–15 minutes from the time of injection.

Formulation: Choline C-11 injection contains 148 MBq to 1225 MBq (4–33.1 mCi/mL) of ¹¹C choline at end of synthesis (EOS) calibration time in aqueous 0.9% sodium chloride solution.

Warnings/Contraindications: Imaging errors have been reported; blood PSA levels < 2 ng/mL have been associated with poor imaging performance. Severe allergic reactions have been reported.

Choline C-11 (Choline C-11, Mayo Clinic PET Radiochemistry Facility) (continued)

Place in Therapy: Studies of men with suspected recurrent prostate cancer and non-informative conventional imaging demonstrated that Choline C-11 imaging returned positive images in at least 50% of patients with histologically-verified prostate cancer.

Notes: Choline C-11 Injection contributes to a patient's long-term cumulative radiation exposure. Ensure safe handling to protect the patient and health care worker.

Poly-Ureaurethane (Nuvail, Innocutis Holdings)

Pharmacology: Liquid Bandage.

Indication: Indicated for managing signs and symptoms of nail dystrophy, ie, nail splitting, nail fragility, for intact or damaged nails.

Adverse Drug Reactions: Stinging upon application.

Dose: Apply to affected nail plate once daily before bedtime.

Formulation: Available as a 16% poly-ureaurethane in organic solvents in a 15 mL bottle.

Warnings/Contraindications: Do not apply directly to deep, open, or profusely bleeding wounds. Persons sensitized to isocyanate should not use this product.

Place in Therapy: Nuvail coats and adheres to the nail surface preventing direct abrasion and friction on the nail surface while also providing protection against the effects of moisture.

Notes: If redness or irritation appears, discontinue use and contact physician Use of other products, eg, ointments, creams and lotions, before application may prevent the film from forming correctly and reduce effectiveness.

Regorafenib (Stivarga, Bayer Healthcare)

Pharmacology: Kinase Inhibitor.

Indication: Indicated for the treatment of patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF therapy, and, if KRAS wild type, an anti-EGFR therapy.

Adverse Drug Reactions: The most common adverse reactions include; asthenia/fatigue, decreased appetite and food intake, hand-foot skin reaction (HFSR)/palmar-plantar erythrodysesthesia (PPE), diarrhea, mucositis, weight loss, infection, hypertension, and dysphonia.

Dose: The recommended dose and schedule is 160 mg orally, once daily for the first 21 days of each 28-day cycle.

Formulation: 40-mg film-coated tablet.

Black box warnings/Contraindications: Severe and sometimes fatal hepatotoxicity has been observed in clinical trials. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue regorafenib for hepatotoxicity as manifested by elevated liver function tests or hepatocellular necrosis, depending upon severity and persistence.

Place in Therapy: The clinical efficacy and safety of regorafenib were evaluated in an international, multi-center, randomized (2:1), double-blind, placebo-controlled trial in 760 patients with previously treated mCRC. The primary efficacy endpoint was overall survival (OS). Patients were randomized to receive 160 mg regorafenib orally once daily (n=505) plus Best Supportive Care (BSC) or placebo (n=255) plus BSC for the first 21 days of each 28-day cycle. The median overall survival in months in patients treated with regorafenib plus BSC was 6.4 compared to 5 months in patients treated with placebo plus BSC.

Notes: Nursing mothers should discontinue drug or nursing, taking into consideration the importance of the drug to the mother.

Perampanel (Fycompa, Eisai Inc.)

Pharmacology: Non-Competitive AMPA Glutamate Receptor Antagonist; Anticonvulsant.

Indication: Adjunctive therapy for the treatment of partial-onset seizures (with or without secondary generalization) in patients aged 12 years and older.

Adverse Drug Reactions: Most common adverse reactions include dizziness, somnolence, fatigue, irritability, falls, nausea, weight gain, vertigo, ataxia, gait disturbance, and balance disorder.

Dose: Recommended starting dose is 2 mg once daily at bedtime in patients not on enzyme-inducing anti-epileptic drugs and 4 mg in patients on enzyme-inducing AEDs. May increase based on clinical response and tolerability by a maximum of 2 mg once daily at bedtime in weekly increments to a dose of 4 mg to 12 mg once daily at bedtime.

Formulation: Available as 2-mg, 4-mg, 6-mg, 8-mg, 10-mg, and 12-mg tablets.

Perampanel (Fycompa, Eisai Inc.) (continued)

Black box warning: Serious or life-threatening psychiatric and behavioral adverse reactions including aggression, hostility, irritability, anger, and homicidal ideation and threats have been reported in patients taking perampanel. Monitor patients for these reactions as well as for changes in mood, behavior, or personality that are not typical for the patient, particularly during the titration period and at higher doses. Perampanel should be reduced if these symptoms occur and should be discontinued immediately if symptoms are severe or are worsening.

Warnings/Contraindications: Suicidal behavior and ideation and neurologic effects have been seen in patients taking perampanel. Monitor for changes in mood and behavior as well as changes in equilibrium, gait, somnolence, and fatigue. There may be an increase in seizure frequency upon withdrawal of medication.

Place in Therapy: The safety and efficacy of perampanel for the adjunctive treatment of partial-onset seizures in adult and pediatric patients was demonstrated in 3, randomized, placebo-controlled, double blind, multicenter trials. The primary endpoint in these studies was the percent change in seizure frequency per 28 days during the treatment period as compared to the baseline period. A statistically significant decrease in seizure rate was observed at doses of 4 to 12 mg per day. Dose response was apparent at 4 to 8 mg with little additional reduction in frequency at 12 mg per day.

Notes: Based on animal data, perampanel may cause fetal harm. Patients should use caution when driving or operating machinery.

Omacetaxine Mepesuccinate (Synribo, Ivax Pharms)

Pharmacology: Antineoplastic Agent, Protein Synthesis Inhibitor.

Indication: Indicated for the treatment of chronic or accelerated phase chronic myeloid leukemia (CML) with resistance and/or intolerance to two or more tyrosine kinase inhibitors.

Adverse Drug Reactions: Most common adverse reactions include thrombocytopenia, anemia, neutropenia, diarrhea, nausea, fatigue, asthenia, injection site reaction, pyrexia, infection, and lymphopenia.

Dose: For induction the manufacturer recommends a dose of 1.25 mg/m² administered by subcutaneous injection twice daily for 14 consecutive days of a 28-day cycle. For maintenance therapy, the manufacturer recommends a dose of 1.25 mg/m² administered by subcutaneous injection twice daily for 7 consecutive days of a 28-day cycle. Dose modifications are needed for toxicity.

Formulation: Available as 3.5-mg single-use vial of lyophilized omacetaxine mepesuccinate.

Warnings/Contraindications: Severe and fatal thrombocytopenia, neutropenia, anemia, increased risk of hemorrhage, glucose intolerance and hyperglycemia including hyperosmolar non-ketotic hyperglycemia have been reported.

Place in Therapy: An increase in survival or improvement in disease-related symptoms has not been proven; the indication for the treatment of CML is based upon response rate. In 2 open-label, non-comparative trials of patients with chronic phase CML and resistance to or intolerance of 2 or more TKIs, treatment with omacetaxine produced a major cytogenetic response in 18.4% of patients with chronic phase CML (n=76) and a major hematologic response in 14.3% of patients with accelerated phase CML (n=35).

Notes: Embryo-fetal toxicity: Can cause fetal harm. Advise females of reproductive potential to avoid pregnancy.

Tofacitinib (Xeljanz, Pfizer Inc.)

Pharmacology: Janus kinase Inhibitor.

Indication: Indicated for the treatment of moderate to severe rheumatoid arthritis in patients with an inadequate response or intolerance to methotrexate.

Adverse Drug Reactions: The most commonly reported adverse reactions were upper respiratory tract infections, headache, diarrhea and nasopharyngitis.

Dose: 5 mg by mouth twice daily.

Formulation: 5-mg tablet.

Black box warning: Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections have occurred. Prior to starting tofacitinib, perform a test for latent tuberculosis. Monitor all patients for active tuberculosis during treatment, even if the initial latent tuberculosis test is negative. Lymphoma and other malignancies have been observed in patients treated with tofacitinib.

Tofacitinib (Xeljanz, Pfizer Inc.) (continued)

Warnings/Contraindications: Use with caution in patients that may be at an increased risk for gastrointestinal perforations. Laboratory monitoring is recommended due to potential changes in lymphocytes, neutrophils, hemoglobin, liver enzymes and lipids.

Place in Therapy: American College of Rheumatology criteria improvement of 20% (ACR20) was demonstrated during 3 placebo-controlled studies in patients (n=1806) treated with tofacitinib citrate with or without background methotrexate therapy.

Notes: Live vaccines should not be given concurrently with tofacitinib. Tofacitinib is not recommended in patients with severe hepatic impairment.

Cabozantinib (Cometriq, Exelixis Inc.)

Pharmacology: Kinase Inhibitor.

Indication: Treatment of progressive, metastatic medullary thyroid cancer (MTC).

Adverse Drug Reactions: The most commonly reported adverse drug reactions ($\geq 25\%$) are diarrhea, stomatitis, palmar-plantar erythrodysesthesia syndrome (PPES), decreased weight, decreased appetite, nausea, fatigue, oral pain, hair color changes, dysgeusia, hypertension, abdominal pain, and constipation.

Dose: The recommended dose of the treatment of MTC is 140 mg by mouth once daily.

Formulation: Available in 20-mg and 80-mg capsules.

Warnings/Contraindications: Black box warning for gastrointestinal perforations occurred in 3% and fistula formation in 1% of cabozantinib treated patients. Severe, sometimes fatal, hemorrhage including hemoptysis and gastrointestinal hemorrhage occurred in 3% of cabozantinib-treated patients. Monitor patients for signs and symptoms of bleeding. Do not administer cabozantinib to patients with severe hemorrhage. Cabozantinib should be discontinued if the patient experiences myocardial infarction, cerebral infarction, or other serious arterial thromboembolic events. Advise women of the potential risk to a fetus.

Place in Therapy: The safety and efficacy of cabozantinib was assessed in an international, multi-center, randomized, double blind, controlled trial of 330 patients with MTC. A statistically significant prolongation in progression-free survival (PFS) was demonstrated among cabozantinib-treated patients compared to those receiving placebo [HR 0.28 (95% CI: 0.19 – 0.40); $p < 0.0001$].

Notes: The most common laboratory abnormalities ($\geq 25\%$) are increased AST, increased ALT, lymphopenia, increased alkaline phosphatase, hypocalcemia, neutropenia, thrombocytopenia, hypophosphatemia, and hyperbilirubinemia.

Pasireotide Diaspartate (Signifor, Novartis Pharms)

Pharmacology: Somatostatin Analog.

Indication: Indicated for the treatment of adult patients with Cushing's disease who cannot undergo pituitary surgery.

Adverse Drug Reactions: Most common reactions include: diarrhea, nausea, cholelithiasis, abdominal pain, fatigue, and diabetes mellitus.

Dose: Recommended initial dose is either 0.6 mg or 0.9 mg subcutaneously twice a day.

Formulation: Available as single-dose ampules in 0.3 mg/mL, 0.6 mg/mL, and 0.9 mg/mL strengths.

Warnings/Contraindications: Decreases in circulating levels of cortisol may occur resulting in biochemical and/or clinical hypocortisolism. Use with caution in patients who are at risk for bradycardia and/or QT prolongations.

Place in Therapy: In a phase 3, multicenter, 12-month, randomized study (n=162), normalization of mean 24-hour urinary free cortisol levels occurred in 15% and 26% of patients who received 6 months of pasireotide diaspartate 0.6 mg and 0.9 mg subcutaneously twice daily, respectively, for the treatment of persistent or recurrent Cushing disease despite pituitary surgery or for whom surgery was not indicated or was refused.

Notes: Intensive glucose monitoring is recommended. Evaluate liver tests prior to and during treatment.

Ponatinib (Iclusig, Ariad Pharmaceuticals)

Pharmacology: Antineoplastic Agent; Tyrosine Kinase Inhibitor.

Indication: Indicated for the treatment of adult patients with chronic phase, accelerated phase, or blast phase chronic myeloid leukemia (CML) or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ALL) that is resistant or intolerant to prior tyrosine kinase inhibitor therapy.

Ponatinib (Iclusig, Ariad Pharmaceuticals) (continued)

Adverse Drug Reactions: The most common adverse reactions included: thrombocytopenia, anemia, neutropenia, lymphopenia, leukopenia, rash, fatigue, headache, dry skin, constipation, arthralgia, nausea, and pyrexia.

Dose: The recommended dose is 45 mg orally once daily with or without food.

Formulation: Available as 15-mg and 45-mg tablets.

Warnings/Contraindications: Black box warning for arterial thrombosis, including fatal myocardial infarction, as well as hepatotoxicity leading to liver failure and death. Monitor hepatic function prior to and during treatment.

Place in Therapy: The efficacy of ponatinib was assessed in a single-arm, open-label, international, multicenter trial. Patients were assigned to one of six cohorts based on disease phase — chronic phase CML (CP-CML), accelerated phase CML (AP-CML), or blast phase CML (BP-CML)/Ph+ALL, resistance or intolerance (R/I) to prior TKI therapy, and the presence of the T315I mutation. The primary efficacy endpoint in CP-CML was major cytogenetic response (MCyR). The primary efficacy endpoint in AP-CML, BP-CML, and Ph+ALL was major hematologic response (MaHR), defined as either a complete hematologic response (CHR) or no evidence of leukemia (NEL). In patients with CP-CML median time to MCyR, in those that achieved it, was 84 days (range: 49 to 334 days). The median time to MaHR in patients with AP-CML, BP-CML, and Ph+ALL was 21 days (range: 12 to 176 days), 29 days (range 12 to 113 days), and 20 days (range: 11 to 168 days), respectively. The median duration of MaHR for patients with AP-CML, BP-CML, and Ph+ALL was 9.5 months (range: 1.1 to 17.7 months), 4.7 months (range: 1.8 to 14.1+ months), and 3.2 months (range: 1.8 to 8.8+ months), respectively.

Notes: There are no trials verifying an improvement in disease-related symptoms or increased survival with ponatinib.

Teduglutide (Gattex, Hospira)

Pharmacology: Glucagon-Like Peptide-2 Analog.

Indication: Indicated in patients with Short Bowel Syndrome (SBS) who are dependent on parenteral support.

Adverse Drug Reactions: The most common adverse reactions include: abdominal pain, injection site reactions, nausea, headaches, abdominal distension, and upper respiratory tract infection.

Dose: The recommended dose of teduglutide is 0.05 mg/kg subcutaneously once daily.

Formulation: Each single-use glass vial contains 5 mg of teduglutide as a white, lyophilized powder for reconstitution with 0.5 mL sterile water for injection provided in a prefilled syringe.

Warnings/Contraindications: Increased risk for the acceleration of neoplastic growth.

Place in Therapy: The efficacy, safety, and tolerability of teduglutide was evaluated in a randomized, double-blind, placebo-controlled, parallel-group, multi-national, multi-center clinical trial in adults with SBS who were dependent on parenteral nutrition/intravenous (PN/IV) support for at least 12 months and required PN at least 3 times per week. The primary efficacy endpoint was based on a clinical response, defined as a subject achieving at least 20% reduction in weekly PN/IV volume from Baseline (immediately before randomization) to both Weeks 20 and 24. The percentages of responders were compared in the intent-to-treat population, which was defined as all randomized patients. Sixty-three percent (27/43) of teduglutide-treated patients versus 30% (13/43) of placebo-treated patients were considered responders ($p=0.002$). At Week 24, the mean reduction in weekly PN/I.V. volume was 4.4 Liters for teduglutide-treated subjects (from pre-treatment baseline of 12.9 Liters) versus 2.3 Liters for placebo-treated subjects (from pre-treatment baseline of 13.2 Liters/week) ($p<0.001$).

Notes: Use within 3 hours after reconstitution and discard any unused medication.

Lomitapide (Juxtapid, Aegerion Pharmaceuticals)

Pharmacology: Microsomal Triglyceride Transfer Protein Inhibitor.

Indication: Indicated as an adjunct to reduce low-density lipoprotein cholesterol, total cholesterol, apolipoprotein B, and non-high-density lipoprotein cholesterol in patients with homozygous familial hypercholesterolemia (HoFH).

Adverse Drug Reactions: Most common adverse reactions include: diarrhea, nausea, dyspepsia, and abdominal pain.

Dose: The recommended initial dose of lomitapide is 5 mg orally once daily.

Formulation: Available as 5-mg, 10-mg, and 20-mg capsules.

Lomitapide (Juxtapid, Aegerion Pharmaceuticals) (continued)

Warnings/Contraindications: Black box warning for increased transaminases as well as an increase in hepatic fat with or without concomitant increases in transaminases. Because of the risk of hepatotoxicity, lomitapide is available only through a restricted program called the Juxtapid REMS Program.

Place in Therapy: The safety and effectiveness of lomitapide as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, were evaluated in a multinational, single-arm, open-label, 78-week trial involving 29 adults with HoFH. After a six week run-in period to stabilize lipid-lowering treatments, including the establishment of LDL apheresis schedule if applicable, lomitapide was initiated at 5 mg daily and titrated to daily doses of 10 mg, 20 mg, 40 mg and 60 mg at weeks 2, 6, 10, and 14, respectively, based on tolerability and acceptable levels of transaminases. The mean percent change in LDL-C from baseline through week 26, the primary endpoint, was -40% representing an average decrease in LDL-C of 190 ± 104 mg/dL.

Notes: The safety and effectiveness of lomitapide has not been established in patients with hypercholesterolemia who do not have HoFH.

Apixaban (Eliquis, Bristol Myers Squibb)

Pharmacology: Factor Xa Inhibitor.

Indication: Indicated to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation.

Adverse Drug Reactions: The most common adverse reactions are related to bleeding.

Dose: The recommended dose is 5 mg orally twice daily.

Formulation: Available as 2.5-mg and 5-mg tablets.

Warnings/Contraindications: Apixaban can cause serious, potentially fatal bleeding.

Place in Therapy: Evidence for the efficacy and safety of apixaban was derived from ARISTOTLE, a multinational, double blind study in patients with non-valvular atrial fibrillation (AF) comparing the effects of apixaban and warfarin on the risk of stroke and non-central nervous system (CNS) systemic embolism. In ARISTOTLE, patients were randomized to apixaban 5 mg orally twice daily (or 2.5 mg twice daily in subjects with at least 2 of the following characteristics: age ≥ 80 years, body weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL) or to warfarin (targeted to an INR range of 2.0 – 3.0). Apixaban was shown to be superior to warfarin at reducing the risk of stroke and systemic embolism. Superiority to warfarin was primarily attributable to a reduction in hemorrhagic stroke and ischemic strokes with hemorrhagic conversion compared to warfarin. Purely ischemic strokes occurred with similar rates on both drugs.

Notes: Apixaban is not recommended in patients with prosthetic heart valves.

Bedaquiline (Sirturo, Janssen Therapeutics)

Pharmacology: Antitubercular Agent; Diarylquinoline Antimycobacterial.

Indication: Indicated as part of combination therapy in adults with pulmonary multi-drug resistant tuberculosis (MDR-TB).

Adverse Drug Reactions: The most common adverse reactions include: nausea, arthralgia, headache, hemoptysis, and chest pain.

Dose: Recommended dose is 400 mg orally once daily for 2 weeks then by 200 mg 3 times per week for 22 weeks.

Formulation: Available as a 100-mg tablet.

Warnings/Contraindications: Use with drugs that prolong the QT interval may cause additive QT prolongation, monitor ECGs more frequently. Hepatic-related adverse drug reactions have been reported with use of bedaquiline. Non-adherence to the treatment regimen could result in failure or resistance.

Place in Therapy: A placebo-controlled, double blind, randomized trial was conducted in treatment-naive patients with multi-drug resistant pulmonary *Mycobacterium tuberculosis* to assess the efficacy of bedaquiline (n=79) or placebo plus other drugs (n= 81). Bedaquiline was administered as 400 mg once daily for the first 2 weeks and as 200 mg 3 times per week for the following 22 weeks. The bedaquiline treatment group the median time to culture conversion was 83 days for the bedaquiline treatment group compared to 125 days for the placebo treatment group.

Notes: Bedaquiline is not indicated for the treatment of latent, extra-pulmonary or drug-sensitive tuberculosis.

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Crofelemer (Fulyzaq, Salix Pharms)

Pharmacology: Antidiarrheal.

Indication: Indicated for the symptomatic relief of non-infectious diarrhea in adult patients with HIV/AIDS on anti-retroviral therapy.

Adverse Drug Reactions: The most common adverse reactions include: upper respiratory tract infections, bronchitis, cough, flatulence and increased bilirubin.

Dose: The recommended dose of crofelemer is 125 mg orally twice a day, with or without food.

Formulation: Available as a 125-mg delayed-release tablet.

Warnings/Contraindications: If infectious etiologies are not considered, there is a risk that patients with infectious etiologies will not receive the appropriate therapy and their disease may worsen.

Place in Therapy: The efficacy of crofelemer 125 mg delayed-release tablets twice daily was evaluated in a randomized, double blind, placebo-controlled (one month) and placebo-free (five month), multi-center study. The study enrolled 374 HIV-positive patients on stable anti-retroviral therapy (ART) with a history of diarrhea for one month or more. In this study, diarrhea was defined as either persistently loose stools despite regular use of anti-diarrheal medication (ADM) (e.g., loperamide, diphenoxylate, and bismuth subsalicylate) or one or more watery bowel movements per day without regular ADM use. In the double-blind period of the study, 136 patients received crofelemer 125 mg twice daily, 54 patients received 250 mg twice daily, 47 patients received 500 mg twice daily, and 138 patients received placebo. The primary efficacy endpoint was the proportion of patients with a clinical response, defined as less than or equal to 2 watery bowel movements per week during at least 2 of the 4 weeks of the placebo-controlled phase. Patients who received concomitant ADMs or opiates were counted as clinical non-responders. A significantly larger proportion of patients in the crofelemer 125 mg twice-daily group experienced clinical response compared with patients in the placebo group (17.6% vs. 8.0%, 1-sided $p < 0.01$).

Notes: Based on animal data, may cause fetal harm.

[\(Back to New Molecular Entities Table\)](#)

<u>NEW BIOLOGICS APPROVALS OF 2012</u>		
(Click on generic drug name for further information)		
GENERIC NAME (BRAND NAME)	SPONSOR	APPROVAL DATE
ZIV-Aflibercept (Zaltrap)	Sanofi-Aventis	Aug 03, 2012
TBO-Filgrastim (Neutroval)	Teva	Aug 29, 2012
Ocriplasmin (Jetrea)	ThromboGenics, Inc.	Oct 17, 2012
Fibrin Sealant Patch (Evarrest)	Omrix Biopharmaceuticals	Dec 5, 2012
Raxibacumab	Human Genome Sciences Inc.	Dec 14, 2012
Influenza Virus Vaccine (Fluarix Quadrivalent)	GlaxoSmithKline	Dec 14, 2012
Immune Globulin Intravenous (Bivigam)	Biotest Pharmaceuticals	Dec 19, 2012
Varicella Zoster Immune Globulin (Varizig)	Cangene Corporation	Dec 20, 2012

ZIV-Aflibercept (Zaltrap, Sanofi-Aventis)

Pharmacology: Antineoplastic Agent; Vascular Endothelial Growth Factor (VEGF) Inhibitor

Indication: For use in combination with 5-fluorouracil, leucovorin, irinotecan-(FOLFIRI) in patients with metastatic colorectal cancer (mCRC) that is resistant to or has progressed following an oxaliplatin-containing regimen.

Adverse Drug Reactions: Most common adverse reactions seen were leukopenia, diarrhea, neutropenia, proteinuria, elevations in transaminases, stomatitis, fatigue, thrombocytopenia, hypertension, weight loss, decreased appetite, epistaxis, abdominal pain, dysphonia, increased serum creatinine, and headache. Adverse reactions, sometimes severe and life-threatening or fatal, have been seen in clinical trials with aflibercept, including: fistula formation, hypertension, arterial thromboembolic events (ATE), proteinuria, neutropenia and neutropenic complications, diarrhea and dehydration, and reversible posterior leukoencephalopathy syndrome (RPLS).

Dose: Administer 4-mg/kg as an intravenous infusion over 1 hour every 2 weeks.

Formulation: Available as single-use vials as 100-mg/4 mL and 200-mg/8 mL.

Warnings/Contraindications: Black box warning for severe and sometimes fatal hemorrhage; including gastrointestinal hemorrhage, gastrointestinal perforation and compromised wound healing. Suspend aflibercept for at least 4 weeks prior to elective surgery, and do not resume for at least 4 weeks following major surgery and until the surgical wound is fully healed.

ZIV-Aflibercept (Zaltrap, Sanofi-Aventis) (continued)

Place in Therapy: A randomized, double-blind, placebo-controlled study in 1226 patients with metastatic colorectal cancer (mCRC) who are resistant to or have progressed during or within 6 months of receiving oxaliplatin-based combination chemotherapy, with or without prior bevacizumab. Patients were randomized to receive either aflibercept or placebo, in combination with 5-fluorouracil plus irinotecan. Median overall survival with placebo/ FOLFIRI was 12.06 months (11.07 to 13.08) n = 614] and with aflibercept/FOLFIRI [13.50 months (12.52 to 14.95) n = 612].

Notes: May cause fetal harm; use highly effective contraception during and up to minimum of 3 months after the last dose. Nursing mothers should discontinue drug or nursing taking into account the importance of the drugs to the mother.

TBO-Filgrastim (Neutroval, Teva Pharma USA)

Pharmacology: Granulocyte Colony-Stimulating Factor.

Indication: Indicated to reduce the duration of severe neutropenia in patients with non-myeloid malignancies who are receiving myelosuppressive anti-cancer agents associated with a clinically significant incidence of febrile neutropenia.

Adverse Drug Reactions: Most common reaction during clinical trial testing was bone pain, with an occurrence of $\leq 1\%$.

Dose: Recommended dose is 5-mcg/kg subcutaneously per day no earlier than 24 hours following myelosuppressive chemotherapy. Daily dosing with tbo-filgrastim should continue until the expected neutrophil nadir is passed and the neutrophil count has recovered to the normal range.

Formulation: Available as 300-mcg/0.5mL and 480-mcg/0.8mL single use prefilled syringes.

Warnings/Contraindications: Do not administer tbo-filgrastim within 24 hours prior to chemotherapy. Splenic rupture and acute respiratory distress syndrome (ARDS) have been associated with the use of tbo-filgrastim, if either is suspected discontinue tbo-filgrastim immediately and treat accordingly. Severe and sometimes fatal sickle cell crises can occur in patients with sickle cell disease receiving human granulocyte colony-stimulating factors. Serous allergic reactions, including anaphylaxis, can occur during treatment with tbo-filgrastim. The administration of antihistamines, steroids, bronchodilators, and/or epinephrine may reduce the severity of the reactions. Tbo-filgrastim should be discontinued and not rechallenged if patient develops a serous allergic reaction.

Place in Therapy: The efficacy of tbo-filgrastim was evaluated in a multinational, multicenter, randomized and controlled phase 3 study in 348 chemotherapy-naive patients with high-risk stage II, stage III, or stage IV breast cancer receiving doxorubicin (60 mg/m²) and docetaxel (75 mg/m²). The study compared tbo-filgrastim to placebo and a non-US-approved filgrastim product. Tbo-filgrastim was associated with a statistically significant reduction in the duration of severe neutropenia as compared to placebo, 1.1 days vs. 3.8 days, respectively (p < 0.0001). It was expected that this agent would be approved under a new abbreviated approval pathway for biosimilar and interchangeable biological products, the implications are that tbo-filgrastim is not considered to be interchangeable with currently available filgrastim formulations.

Notes: Pregnancy category C. The safety and effectiveness of tbo-filgrastim have not been established in patients less than 18 years of age.

Ocriplasmin (Jetrea, ThromboGenics, Inc)

Pharmacology: Vitreolytic.

Indication: Indicated for the treatment of symptomatic vitreomacular adhesion.

Adverse Drug Reactions: The most commonly reported reactions include vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment, and retinal edema.

Dose: The recommended dose is 0.125 mg by intravitreal injection once as a single dose.

Formulation: Available as a single-use glass vials containing 0.5mg/0.2mL solution.

Warnings/Contraindications: Decreases in vision due to progression of the condition with traction which may require surgical intervention. Patients should be monitored and instructed to report any symptoms without delay. The potential for lens subluxation is possible while using ocriplasmin.

Place in Therapy: In two randomized, placebo-controlled trials of patients with vitreomacular adhesion (n=652), significantly more patients achieved nonsurgical resolution of adhesion and total posterior vitreous detachment after intravitreal injection of ocriplasmin compared with those receiving placebo.

Notes: Must dilute before use. For single use ophthalmic intravitreal injection only.

Fibrin Sealant Patch (Evarrest, Omrix Biopharmaceuticals)

Pharmacology: Blood Product Derivative; Human Fibrinogen and Human Thrombin.

Indication: Indicated for use with manual compression as an adjunct to hemostasis for soft tissue bleeding during open retroperitoneal, intra-abdominal, pelvic, and non-cardiac thoracic surgery when control of bleeding by standard surgical methods of hemostasis (e.g., suture, ligature, cautery) is ineffective or impractical.

Adverse Drug Reactions: The most common adverse reactions reported include: abdominal distension, blood fibrinogen increased, post procedural and intra-abdominal hemorrhage, and pulmonary embolism.

Dose: For topical use on soft tissue bleeding only. Determine the number of patches to be applied based upon the surface area and anatomic location of the bleeding tissue to be treated. Keep the patch dry until use. Place the powdery (active) side of the patch on the surface of tissue. Apply immediate manual compression over the entire surface of the patch and maintain contact pressure for 3 minutes to control the bleeding.

Formulation: The Evarrest Patch consists of human fibrinogen and human thrombin embedded in a flexible composite patch component. The active side is powdery, and the non-active side has an embossed wave pattern.

Warnings/Contraindications: Do not use to treat bleeding from large defects in arteries or veins. This product should not be applied intravascularly. Do not use in individuals known to have anaphylactic or severe systemic reaction to human blood products. Avoid use in closed spaces (i.e., in, around, or in proximity to, foramina in bone or areas of bony confine) where swelling may cause compression. Thrombosis can occur if absorbed systemically. Apply topically to soft tissue bleeding only.

Place in Therapy: Controlled studies evaluating benefits of fibrin sealant preparations compared to standard care in various settings are scarce; of those available, many suffer from design deficiencies, which may have contributed to the equivocal results observed in some instances. Commercial formulations are preferred over autologous or "homemade" products. Cost should be considered in the selection process, as efficacy of available preparations appears similar.

Notes: This product is not intended for use in children under one month of age. Everest patch should not be used in lieu of sutures or other forms of mechanical ligation in the treatment of major arterial or venous bleeding. Because this product is made from human blood, it may carry a risk of transmitting infectious agents — e.g., viruses, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

Raxibacumab (Raxibacumab, Human Genome Sciences Inc.)

Pharmacology: Monoclonal Antibody.

Indication: Indicated for the treatment of adult and pediatric patients with inhalational anthrax due to *Bacillus anthracis* in combination with appropriate antibacterial drugs, as well as prophylaxis of inhalational anthrax when alternative therapies are not available or are not appropriate.

Adverse Drug Reactions: Common adverse reactions include: rash, pain in extremity, pruritus, and somnolence.

Dose: Dilute and administer as an intravenous infusion (IV) over 2 hours and 15 minutes. The recommended dose is based upon weight — Adults: 40 mg/kg; pediatrics > 50 kg: 40 mg/kg; pediatrics 15 kg to 50 kg: 60 mg/kg; and pediatrics 15 kg or less: 80 mg/kg.

Formulation: Single-use vial contains 1700 mg/34 mL (50 mg/mL) raxibacumab solution.

Warnings/Contraindications: Infusion reactions may occur; patients should be pre-medicated with diphenhydramine.

Place in Therapy: Raxibacumab's effectiveness in treating inhalational anthrax was demonstrated in one study in monkeys and three studies in rabbits. All animals were administered aerosolized *B. anthracis* spores, and efficacy was determined by survival at the end of the studies. Animals received varying doses of raxibacumab, placebo or antibiotics normally used to treat anthrax.

Notes: Caution should be exercised when administered to a nursing woman.

Influenza Virus Vaccine (Fluarix Quadrivalent, GlaxoSmithKline)

Pharmacology: Vaccine; Inactivated (Viral).

Indication: Indicated for active immunization for the prevention of disease caused by influenza A subtype viruses and type B viruses contained in the vaccine in person 3 years of age and older

Adverse Drug Reactions: In adults, the most common adverse reactions include: injection site adverse reaction was pain; the most common systemic adverse events were muscle aches, headache, and fatigue. In children 3 through 5 years of age, the most common systemic adverse events were drowsiness, irritability, and loss of appetite.

Influenza Virus Vaccine (Fluarix Quadrivalent, GlaxoSmithKline) (continued)

Dose: Patients who are 3 through 8 years of age that have not previously been vaccinated should receive two doses (0.5 mL) at least 4 weeks apart. Patients who are 3 through 8 years of age who have previously been vaccinated should receive 1 to 2 doses depending on vaccination history per the annual Advisory Committee on Immunization Practices (ACIP). Persons 9 years of age and older should receive one dose of 0.5 mL. Please see full prescribing information for more information regarding the dosing of Fluarix.

Formulation: Available as a suspension for injection supplied in 0.5-mL single-dose prefilled syringes.

Warnings/Contraindications: History of severe allergic reactions (e.g., anaphylaxis) to any component of the vaccine, including egg protein, or following a previous dose of any influenza vaccine. If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior influenza vaccine, the decision to give Fluarix should be based on careful consideration of potential benefits and risks.

Place in Therapy: Studies comparing Fluarix Quadrivalent to other trivalent influenza immunizations have not been performed. Efficacy data is based on Fluarix Trivalent.

Notes: To be administered by intramuscular injection only.

Immune Globulin Intravenous (Bivigam, Biotest Pharmaceuticals)

Pharmacology: Blood Product Derivative; Immune Globulin.

Indication: Indicated for the treatment of primary humoral immunodeficiency (PI).

Adverse Drug Reactions: The most common adverse reactions reported include: headache, fatigue, infusion site reaction, nausea, sinusitis, blood pressure increased, diarrhea, dizziness, and lethargy.

Dose: For the treatment of PI administer 300 – 800 mg/kg every 3 – 4 weeks with an initial infusion rate of 0.5 mg/kg/min for the first 10 minutes — increase every 20 minutes, if tolerated, by 0.8 mg/kg/min up to 6 mg/kg/min.

Formulation: Available as a liquid solution containing 10% IgG (100mg/mL).

Warnings/Contraindications: Black box warning for increased risk of renal dysfunction, acute renal failure, osmotic nephrosis, and death in predisposed patients. For patients at risk of renal dysfunction or failure, administer immune globulin intravenous (IGIV) at the minimum dose recommended and the minimum infusion rate practicable. IGIV is contraindicated in patients with a history of anaphylactic or severe systemic reactions to human immunoglobulin as well in patients with IgA deficiency with antibodies to IgA and a history of hypersensitivity. Thrombotic events have occurred in patients receiving IGIV therapy, monitor patients with known risk factors for thrombotic events. Hyperproteinemia, increased serum viscosity, and hyponatremia or pseudohyponatremia can occur in patients receiving IGIV therapy.

Place in Therapy: The efficacy of Bivigam for the treatment of PI was evaluated in a trial of 63 patents that received 300 – 800 mg/kg every 3 – 4 weeks for approximately 1 year. The primary endpoint of the study was the rate of serous bacterial infection, which occurred in two patients at a rate of 0.037 per year.

Notes: Because this product is made from human blood, it may carry a risk of transmitting infectious agents — e.g., viruses, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

Varicella Zoster Immune Globulin (Varizig, Cangene Corporation)

Pharmacology: Immune Globulin.

Indication: Indicated for post-exposure prophylaxis to reduce the severity of varicella in high-risk individuals including; immunocompromised children and adults, newborns of mothers with varicella shortly before or after delivery, premature infants, infants less than one year of age, adults without evidence of immunity, and pregnant women.

Adverse Drug Reactions: Most common adverse reactions from clinical trials are pain at the injection and headache.

Dose: Dosing is based upon body weight and is available in the full prescribing information

Formulation: Available as a lyophilized powder for solution as single-use vials of 125 units.

Warnings/Contraindications: History of anaphylactic or severe systemic reactions to human globulins IgA-deficient patients with antibodies against IgA and a history of hypersensitivity.

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Varicella Zoster Immune Globulin (Varizig, Cangene Corporation) (continued)

Place in Therapy: A randomized, open-label, multicenter, active controlled clinical trial was conducted in 60 pregnant women without immunity to VZV. Patients were stratified based on the time since exposure to varicella and randomized into one of three doses. It was found that symptoms were similar across all groups and none of the subjects had serious complications of varicella. The small number of subjects in each treatment stratum and the lack of agreed upon pre-specified hypothesis testing precluded formal statistical comparisons between groups. It is not known whether use of varicella zoster immune globulin will reduce the incidence of chickenpox infection after exposure to VZV, or whether it will modify the course of an established VZV infection.

Notes: Varicella zoster immune globulin is for intramuscular administration only.

[\(Back to New Biologic Approvals Table\)](#)

<u>NEW DRUG FORMULATIONS / COMBINATIONS OF JULY – DECEMBER 2012</u>			
(Click on generic drug name for further information)			
GENERIC NAME (BRAND NAME)	SPONSOR	CATEGORY	APPROVAL DATE
Minocycline, Extended-Release (Ximino)	Ranbaxy	3S	July 11, 2012
Phentermine/Topiramate ER (Qsymia)	Vivus	4S	July 17, 2012
Prednisone, Delayed-Release (Rayos)	Horizon Pharma	3S	July 26, 2012
Vincristine Liposome Injection (Marqibo)	Talon Therapeutics	5S	Aug 9, 2012
Sildenafil Suspension (Revatio)	Pfizer	3P	Aug 30, 2012
Everolimus (Afinitor Disperz)	Novartis	3P	Aug 29, 2012
Methylphenidate HCl (Quillivant XR)	Nextwave Pharms Inc.	3S	Sept 27, 2012
Loteprednol Etabonate (Lotemax)	Bausch & Lomb	3S	Sept 28, 2012
Cysteamine (Cystaran)	Sigma Tau	3P	Oct 02, 2012
Oxcarbazepine ER (Oxtellar XR)	Supernus Pharma Inc.	3S	Oct 19, 2012
Tapentadol Oral Solution (Nucynta)	Janssen Pharma	3S	Oct 15, 2012
Leuprolide Acetate; Norethindrone Acetate (Lupaneta Pack)	Abbott Laboratories	4S	Dec 14, 2012
Clobazam (Onfi)	Lundbeck LLC	3S	Dec 14, 2012
Loxapine (Adasuve)	Alexza Pharms	3S	Dec 21, 2012

Minocycline, Extended-Release (Ximino, Ranbaxy)

Pharmacology: Tetracycline Antibiotic.

Indication: Indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris in patients 12 years of age and older.

Dose: 1 mg/kg daily for 12 weeks. In patients with renal impairment, the total dosage should be decreased by either reducing the recommended individual doses and/or by extending the time intervals between doses.

Formulation: Available in 45-mg, 67.5-mg, 90-mg, 112.5-mg and 135-mg extended release capsules.

Place in Therapy: The main clinical benefit of minocycline in the treatment of acne is its effect on *Propionibacterium acnes*. Minocycline has been shown to be effective in the treatment of acne vulgaris, but has not shown a benefit on non-inflammatory lesions during clinical trial testing.

Phentermine/Topiramate, Extended-Release (Qsymia, Vivus)

Pharmacology: Sympathomimetic Amine Anorectic and Antiepileptic.

Indication: Indicated as an adjunct to a reduced-calorie diet and increase physical activity for chronic weight management in adults with an initial body mass index (BMI) of 30-kg/m² or 27-kg/m² in the presence of at least one weight-related comorbidity such as hypertension, type-2 diabetes, or dyslipidemia.

Phentermine/Topiramate, Extended-Release (Qsymia, Vivus) (continued)

Dose: The recommended dose of phentermine/topiramate is 3.75-mg/23-mg daily for 14 days; which can then be increased to 7.5-mg/46-mg daily. Phentermine/topiramate should be discontinued if 3% or 5% weight loss is not achieved in 12 weeks with 7.5-mg/46-mg dose or 15-mg/92-mg, respectively. Do not exceed 7.5mg/46mg dose for patients with moderate or severe renal impairment or patients with moderate hepatic impairment. In patients with moderate or severe renal impairment or with moderate hepatic impairment, do not exceed phentermine 7.5mg/topiramate 46mg per day.

Formulation: Available as an extended-release capsule in the following strengths: 3.75-mg/2-mg , 7.5-mg/46-mg, 11.25-mg/69-mg, 15-mg/92-mg (phentermine/topiramate).

Place in Therapy: Phentermine/topiramate represents an additional medication to the already commercially available products for chronic weight management.

Prednisone, Delayed-Release (Rayos, Horizon Pharma)

Pharmacology: Synthetic Adrenocortical Steroid.

Indication: Indicated as an anti-inflammatory or immunosuppressive agent for certain allergic, dermatologic, gastrointestinal, hematologic, ophthalmologic, nervous system, renal, respiratory, rheumatologic, specific infectious diseases or conditions and organ transplantation. Prednisone delayed-release (DR) is also indicated for the treatment of certain endocrine conditions and palliation of certain neoplastic conditions.

Dose: The timing of administration should take into account the delayed-release pharmacokinetics and the disease or condition being treated: The initial dosage may vary from 5 to 60-mg per day depending on the specific disease, disease severity and patient response. Patients currently taking immediate-release prednisone, prednisolone, or methylprednisolone should be switched to prednisone DR at an equivalent dose based on relative potency.

Formulation: Available as 1-mg, 2-mg and 5-mg delayed release tablets.

Place in Therapy: Prednisone is generally considered the glucocorticoid of choice for anti-inflammatory or immunosuppressant effects. The delayed release formulation has approximately a 4-hour time lag when taken with food compared with immediate-release formulations, but absorption, distribution, and elimination are comparable.

Vincristine Liposome Injection (Marqibo, Talon Therapeutics)

Pharmacology: Vinca Alkaloid.

Indication: Indicated for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies.

Dose: Administer at a dose of 2.25-mg/m² intravenously over 1 hour once every 7 days.

Formulation: The final drug product is prepared on site from the components in the vincristine sulfate liposome kit. After preparation, each single-dose vial of vincristine sulfate liposome injection contains 5-mg/31mL (0.16-mg/mL) vincristine sulfate.

Place in Therapy: Clinical data are too limited at present to address the place of liposomal vincristine. Overall, the formulation may be more effective than conventional (free) vincristine in some malignancies without an increase in toxicity.

Sildenafil Suspension (Revatio, Pfizer)

Pharmacology: Phosphodiesterase-5 (PDE-5).

Indication: Indicated for the treatment of pulmonary arterial hypertension (WHO Group I) in adults to improve exercise ability and delay clinical worsening.

Dose: Tablets and oral suspension: 20 mg three times a day by mouth, 4-6 hours apart. Injection: 10 mg (12.5 mL) three times a day as an intravenous bolus injection.

New Formulation: Oral Suspension.

Place in Therapy: Delayed clinical worsening was shown in patients stabilized on intravenous epoprostenol in a randomized, double-blind, placebo-controlled clinical study (n=267).

Everolimus (Afinitor Disperz, Novartis)

Pharmacology: Kinase Inhibitor.

Indication: Indicated for the treatment of pediatric and adult patients with tuberous sclerosis complex (TSC) who have subependymal giant cell astrocytoma (SEGA) that requires therapeutic intervention but cannot be curatively resected.

[\(Back to New Drug Formulations/Combinations Table\)](#)

Everolimus (Afinitor Disperz, Novartis) (continued)

Dose: HR+BC, advanced PNET, advanced RCC, or renal angiomyolipoma with TSC: 10 mg once daily with or without food. SEGA with TSC: 4.5 mg/m² once daily; adjust dose to attain trough concentrations of 5-15 ng/mL.

New Formulation: Everolimus tablets for oral suspension are available as 2 mg, 3 mg, and 5 mg tablets for oral suspension.

Place in Therapy: Represents a new dosage form available to pediatric patients. The effectiveness of both the tablets and tablets for oral suspension is based on demonstration of durable objective response, as evidenced by reduction in SEGA tumor volume. Improvement in disease-related symptoms and overall survival in patients with SEGA and TSC has not been demonstrated.

Methylphenidate (Quillivant XR, Nextwave Pharms Inc.)

Pharmacology: Central Nervous System (CNS) stimulant.

Indication: Attention Deficit Hyperactivity Disorder (ADHD).

Dose: For patients 6 years and above, recommended starting dose is 20 mg given orally once daily in the morning. Dosage may be increased weekly in increments of 10 mg to 20 mg per day. Daily dosage above 60 mg is not recommended.

New Formulation: Extended-release oral suspension 25 mg/5 mL (after reconstitution with water).

Loteprednol Etabonate (Lotemax, Bausch & Lomb)

Pharmacology: Corticosteroid.

Indication: Post-operative inflammation and pain following ocular surgery.

Dose: Apply one to two drops into the conjunctival sac of the affected eye four times daily beginning the day after surgery and continuing throughout the first two weeks of the post-operative period.

New Formulation: Sterile preserved ophthalmic gel.

Cysteamine (Cystaran, Sigma Tau)

Pharmacology: Cystine-Depleting Agent.

Indication: Indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

Dose: Instill one drop in each eye, every waking hour.

New Formulation: Sterile ophthalmic solution containing 6.5 mg/mL of cysteamine hydrochloride.

Oxcarbazepine ER (Oxtellar XR, Supernus Pharma Inc)

Pharmacology: Anticonvulsants.

Indication: Adjunctive therapy in the treatment of partial seizures in adults and children aged 6 to 17 years of age.

Dose: The recommended daily dose is 1,200 mg to 2,400 mg once per day.

New Formulation: Available as 150 mg, 300 mg and 600 mg extended-release tablet.

Tapentadol Oral Solution (Nucynta, Janssen Pharma)

Pharmacology: Opioid Analgesic.

Indication: Indicated for the management of moderate to severe acute pain in adults.

Dose: Initiate tapentadol with or without food at a dose of 2.5 mL (50 mg), 3.75 mL (75 mg), or 5 mL (100 mg) every 4 to 6 hours depending upon pain intensity. On the first day of dosing, the second dose may be administered as soon as one hour after the first dose, if adequate pain relief is not attained with the first dose.

New Formulation: Available as 20 mg/mL oral solution.

Leuprolide Acetate; Norethindrone Acetate (Lupaneta Pack, Abbott Endocrine)

Pharmacology: Gonadotropin-Releasing Hormone (Gnrh) Agonist and Progestin.

Indication: Initial management of painful symptoms of endometriosis and the management of recurrence of symptoms

Dose: Leuprolide acetate for depot suspension 11.25 mg given by a healthcare provider as a single intramuscular injection every 3 months for up to two injections (6 months of therapy). Norethindrone acetate 5 mg tablets taken orally by the patient once per day for up to 6 months

New Formulation: The Lupaneta pack contains 11.25 mg of leuprolide acetate for suspension and a 90 count bottle of 5-mg norethindrone acetate.

[\(Back to New Drug Formulations/Combinations Table\)](#)

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Clobazam (Onfi, Lundbeck)

Pharmacology: Benzodiazepine.

Indication: Adjunctive treatment of seizures associated with Lennox-Gastaut syndrome in patient's ≥ 2 years of age.

Dose: Patients ≤ 30 kg should receive 5 mg orally daily and titrate as tolerated up to 20 mg daily. In patients > 30 kg, initiate at 10 mg daily by mouth and titrate as tolerated up to 40 mg daily.

New Formulation: Available as a 2.5 mg/mL oral suspension in 120 mL bottles.

Loxapine (Adasuve, Alexza Pharmaceuticals)

Pharmacology: Typical Antipsychotic.

Indication: Acute treatment of agitation associated with schizophrenia or bipolar I disorder in adults.

Dose: The recommended dose for acute agitation is 10 mg administered by oral inhalation, using a single-use inhaler.

New Formulation: Available as a 10 mg powder for inhalation in a single-use inhaler.

[\(Back to New Drug Formulations/Combinations Table\)](#)

<u>NEW DRUG INDICATIONS OF 2012</u>		
(Click on generic drug name for further information)		
GENERIC NAME (BRAND NAME)	SPONSOR	APPROVAL DATE
Emtricitabine/Tenofovir Disoproxil Fumarate (Truvada)	Gilead Sciences, Inc.	July 16, 2012
Everolimus (Afinitor)	Novartis	July 20, 2012
Ranibizumab (Lucentis)	Boehringer Ingelheim	Aug 10, 2012
Linagliptin (Tradjenta)	Boehringer Ingelheim	Aug 13, 2012
Adalimumab (Humira)	Abbott	Sept 28, 2012
Paclitaxel (Abraxane)	Abraxis BioScience	Oct 11, 2012
Rivaroxaban (Xarelto)	Janssen Pharms	Nov 02, 2012
Eltrombopag (Promacta)	GlaxoSmithKline	Nov 16, 2012
Abiraterone Acetate (Zytiga)	Janssen Biotech	Dec 10, 2012

Emtricitabine/Tenofovir Disoproxil Fumarate (Truvada, Gilead Sciences, Inc.)

Pharmacology: Nucleoside Analog HIV-1 Reverse Transcriptase Inhibitors

New Indication: Emtricitabine/tenofovir is indicated in combination with safer sex practices for pre-exposure prophylaxis (PrEP) to reduce the risk of sexually acquired HIV-1 in adults at high risk.

Dose: Recommended dose in HIV-1 uninfected adults is one tablet (200mg emtricitabine and 300mg of tenofovir) orally once daily taken with or without food. Manufacturer does not recommend use in patients with a CrCl below 60 mL/min.

Everolimus (Afinitor, Novartis)

Pharmacology: Kinase Inhibitor.

New Indication: Treatment of postmenopausal women with advanced hormone receptor-positive, human epidermal growth factor receptor type 2 (HER-2) negative breast cancer in combination with exemestane, after failure of treatment with letrozole or anastrozole.

Dose: The recommended adult dose of everolimus for the treatment of postmenopausal women with advanced hormone receptor-positive, HER-2-negative breast cancer in combination with exemestane after failure of treatment with letrozole or anastrozole is 10 mg orally once daily. Reduce the dose of everolimus in patient with hepatic impairment. If moderate inhibitors of CYP3A4 and/or P-glycoprotein (PgP) are required, reduce the dose to 2.5 mg once daily; if tolerated, consider increasing to 5 mg once daily. If strong inducers of CYP3A4 are required, increase the dose of everolimus in 5 mg increments to a maximum of 20 mg once daily.

Ranibizumab (Lucentis, Genentech)

Pharmacology: Monoclonal Antibody; Vascular Endothelial Growth Factor (VEGF) Inhibitor.

New Indication: The treatment of diabetic macular edema (DME).

Dose: The manufacturer recommends 0.3-mg administered by intravitreal injection approximately every 28 days.

[\(Back to New Drug Indications Table\)](#)

Linagliptin (Tradjenta, Genentech)

Pharmacology: Dipeptidyl peptidase-4 (DPP-4) Inhibitor.

New Indication: Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin

Dose: Recommended dose is 5 mg daily, when linagliptin is used in combination with an insulin secretagogue (e.g., sulfonylurea) or with insulin, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia.

Adalimumab (Humira, Abbott)

Pharmacology: Tumor Necrosis Factor (TNF) Blocker.

New Indication: Inducing and sustaining clinical remission in adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to immunosuppressants (e.g., corticosteroids, azathioprine or 6-mercaptopurine).

Dose: Initial dose (Day 1): 160 mg (four 40 mg injections in one day or two 40 mg injections per day for two consecutive days). Second dose two weeks later (Day 15): 80 mg. Two weeks later (Day 29): Begin a maintenance dose of 40 mg every other week.

Paclitaxel (Abraxane, Abraxis BioScience)

Pharmacology: Microtubule Inhibitor.

New Indication: Indicated for patients with locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC), as first-line treatment in combination with carboplatin in patients who are not candidates for curative surgery or radiation therapy.

Dose: The recommended dose of paclitaxel is 100 mg/m² IV over 30 minutes on Days 1, 8, and 15 of each 21-day cycle.

Rivaroxaban (Xarelto, Janssen Pharms)

Pharmacology: Factor Xa Inhibitor.

New Indication: Indicated for the treatment and/or reducing the risk of recurrent DVT, and PE.

Dose: 15 mg orally twice daily with food for the first 21 days for the initial treatment of acute DVT or PE. After the initial treatment period, administer 20 mg orally once daily with food for the remaining treatment and the long-term reduction in the risk of recurrence of DVT and of PE.

Eltrombopag (Promacta, GlaxoSmithKline)

Pharmacology: Thrombopoietin Receptor Agonist.

New Indication: Indicated for the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy.

Dose: Initiate at 25 mg once daily for all patients. Adjust to achieve a target platelet count required to initiate antiviral therapy. Do not exceed a daily dose of 100 mg.

Abiraterone Acetate (Zytiga, Janssen Biotech)

Pharmacology: Antineoplastic Agent; CYP17 inhibitor.

New Indication: Indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.

Dose: The recommended dose of abiraterone is 1,000 mg (four 250 mg tablets) administered orally once daily in combination with prednisone 5 mg orally twice daily.

[\(Back to New Drug Indications Table\)](#)

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References: Available upon request