New Molecular Entities of January to June 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.

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<td>1. New molecular entity - drug not marketed in U.S. by any manufacturer</td>
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Ingenol Mebutate (Picato®, Leo Pharma)
Pharmacology: Topical inducer of cell death.
Indication: Topical treatment of actinic keratosis.
Adverse Drug Reactions: Local skin reactions including; pain, pruritus, irritation, and infection at the applications site. Periorbital edema, nasopharyngitis, headache have also been reported.
Dose: Face/Scalp: Apply 0.015% gel to the affected area once daily for 3 days; Trunk/Extremities: Apply 0.05% gel to the affected area once daily for 2 days.
Formulation: Available as a 0.015% and 0.05% gel.
Warnings/Contraindications: No contraindications. Avoid contact with the periorcular area. Eye disorders including; severe eye pain, eyelid edema, eyelid ptosis, and periorbital edema have been associated with ingenol mebutate. If exposure occurs, flush eyes with water and seek medical care. Local skin reactions (vesiculation/postulation and erosion/ulceration) can occur. Administration of ingenol mebutate gel is not recommended until skin is healed from any previous drug or surgical treatment.
Place in Therapy: The short treatment course for ingenol mebutate makes it unique among current options.
Notes: Allow the treated area to dry for 15 minutes after application. Avoid washing/touching the treated area for 6 hours after treatment. Also, avoid activities that cause excessive sweating. The patient may wash the treatment area with a mild soap 6 hours after application.

Axitinib (Inlyta®, Pfizer)
Pharmacology: Antineoplastic Agent, Tyrosine Kinase Inhibitor, Vascular Endothelial Growth Factor (VEGF) Inhibitor.
Indication: Advanced renal cell carcinoma after failure of one prior systemic therapy.
Adverse Drug Reactions: Common reactions include diarrhea, hypertension, fatigue, decreased appetite/weight loss, nausea, dysphonia, palmar/plantar erythrodynesthesia (hand-foot syndrome), vomiting, asthenia, and constipation.
Dose: 5 mg every 12 hours with a full glass of water (Do not take with food).
Formulation: Available as a 1-mg and 5-mg tablet.
Warnings/Contraindications: No contraindications listed by the manufacturer. Monitor for hypertension and treat as needed. For persistent hypertension, reduce the dose of axitinib. Use with caution in patients who are at risk for thrombotic events. Because hemorrhagic events have been reported, axitinib should not be used in patients with evidence of untreated brain metastasis or recent active gastrointestinal bleeding. Use with caution in patients at risk for gastrointestinal perforation or fistula. Because hypothyroidism has been reported, thyroid function should be monitored before starting and throughout treatment. Stop axitinib at least 24 hours prior to scheduled surgery. Reversible Posterior Leukoencephalopathy Syndrome (RPLS) has been reported. Permanently discontinue axitinib if signs or symptoms of RPLS occur. Monitor for proteinuria before starting and throughout treatment. Monitor ALT, AST, and bilirubin before starting and throughout treatment. Axitinib can cause fetal harm when administered to a pregnant woman.
Axitinib (Inlyta®, Pfizer) continued

Place in Therapy: Axitinib was compared to sorafenib in a randomized open-label clinical trial in 723 patients whose disease progressed on or after treatment with prior systemic therapy. A significant difference in progression-free survival was seen between axitinib and sorafenib, median 6.7 months versus 4.7 months, respectively. No difference between overall survival was demonstrated.

Notes: The starting dose of axitinib should be decreased if used in patients with moderate hepatic impairment. Axitinib has not been studied in patients with severe hepatic impairment. Avoid strong CYP3A4 or CYP3A5 inhibitors and reduce the axitinib dose if concomitant therapy with such medications is unavoidable. Women of childbearing potential should be advised of the potential hazard to the fetus and should avoid becoming pregnant while receiving treatment.

Vismodegib (Erivedge®, Genentech Inc)

Pharmacology: Antineoplastic, Hedgehog pathway inhibitor.
Indication: Metastatic basal cell carcinoma or in patients with locally advanced basal cell carcinoma that has recurred following surgery or for patients that are not candidates for surgery or radiation.
Adverse Drug Reactions: gastrointestinal reactions are common and include; nausea, constipation, diarrhea, vomiting, and anorexia. Other reported reactions include; muscle spasms, arthralgia, dysgeusia, ageusia, alopecia, weight loss, and fatigue.
Dose: 150 mg by mouth once daily until disease progression or unacceptable toxicity.
Formulation: Available as 150-mg capsules
Warnings/Contraindications: Black box warning for risks of intrauterine fetal death, male-mediated teratogenicity, and pregnancy. Male patients should be advised of potential vismodegib exposure in semen. Blood donation or blood product donation is not recommended during therapy and at least for 7 months after the last dose. Vismodegib’s safety and efficacy has not been determined in neonates, infants, children, or adolescents.
Place in Therapy: Vismodegib is the first hedgehog pathway inhibitor available on the market. The safety and efficacy was shown in a single arm, open-label two-cohort trial involving 104 patients that had metastatic basal cell carcinoma (mBCC) (n = 33) or locally advanced BCC (laBCC) (n = 71) taking 150mg of cimodegib per day. The response rate was 30.3% in subjects with mBCC and 42.9% in subjects with laBCC.
Notes: Administer with or without food. Swallow capsule whole; do not crush, chew, or open capsules. If a dose is missed, an additional dose is not to be taken; resume normal dosing schedule. Pregnancy status of all female patients should be verified within 7 days prior to starting vismodegib therapy.

Ivacaftor (Kalydeco®, Vertex Pharms)

Pharmacology: Cystic fibrosis transmembrane conductance regulator (CFTR) potentiator.
Indication: Cystic fibrosis (CF) in patients 6 years and older who have a G551D mutation.
Adverse Drug Reactions: Most commonly occurring adverse effects included; headache, oropharyngeal pain, upper respiratory tract infection, nasal congestion, abdominal pain, nasopharyngitis, diarrhea, rash, nausea, dizziness
Dose: Take 150 mg every 12 hours with a high fat meal. Reduce dose in moderate to severe hepatic impairment or when administered with moderate to strong CYP3A4 inhibitors.
Formulation: 150 mg tablet.
Warnings/Contraindications: No contraindications listed by the manufacturer. ALT/AST should be assessed prior to initiating therapy, every 3 months during the first year of therapy, and annually after the first year. Ivacaftor should be discontinued if transaminase levels increase greater than 5 times the upper limit of normal. Once transaminase levels resolve, ivacaftor may be restarted if the benefits outweigh the risks. If administered with strong CYP3A4 inhibitors, reduce ivacaftor dose to 150 mg twice weekly and when administered with moderate CYP3A4 inhibitors reduce dose to 150 mg once daily. Avoid grapefruit and Seville oranges when taking ivacaftor.
Place in Therapy: The safety and efficacy of ivacaftor towards improving lung function in CF patients with the G551D mutation was demonstrated in two randomized, double-blind, placebo-controlled trials involving 213 clinically stable patients. FDA-cleared CF mutation test should be used to test the presence of the G551D mutation because ivacaftor is not effect for patients that are homozygous for the F508del mutation.

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**Tafluprost (Zioptan®, Merck Sharp & Dohme Corp)**

**Pharmacology:** Prostaglandin analog.

**Indication:** Increased intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

**Adverse Drug Reactions:** Macular edema (including cystoid macular edema), conjunctival hyperemia, ocular irritation/stinging/pruritus/pain, increased eyelash pigmentation, hyperpigmentation of periorbital tissue.

**Dose:** Instill 1 drop in the conjunctival sac of the affected eye(s) once daily in the evening.

**Formulation:** 0.0015% ophthalmic solution.

**Warnings/Contraindications:** Tafluprost should be used with caution in patients with active intraocular inflammation, aphakia, pseudophakic patients with a torn lens, and patients with known risk factors for macular edema. Safety and efficacy has not been established in neonates, infants, children, and adolescents.

**Place in Therapy:** Tafluprost is a preservative free formulation and may represent an alternative option for patients who cannot tolerate preservative-containing products. Tafluprost was shown to be non-inferior to latanoprost in reducing intraocular pressure in a 24-month controlled clinical trial.

**Notes:** Tafluprost is for ophthalmic use only. Advise patients to tilt their head back slightly and pull the lower eyelid down with the index finger to form a pouch. Squeeze one drop into the pouch, close eyes gently for 1 to 2 minutes, and do not blink. This product does not contain preservatives and may be use concomitantly with other intraocular pressure reducing agents.

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**Lucinactant (Surfaxin®, Discovery Laboratories, Inc.)**

**Pharmacology:** Endogenous pulmonary surfactant.

**Indication:** Prevention of respiratory distress syndrome (RDS) in premature infants at high risk for RDS.

**Adverse Drug Reactions:** Administration related reactions like endotracheal tube reflux, pallor, endotracheal tube obstruction, and need for dose interruption.

**Dose:** Administer 5.8mL per kg birth weight via endotracheal tube. A maximum of 4 doses can be administered during the first 48 hours of life given no more frequently than every 6 hours.

**Formulation:** 8.5 mL intratracheal suspension

**Warnings/Contraindications:** Lucinactant can rapidly change lung compliance and oxygenation. Lucinactant should be administered only by clinicians trained and experienced in resuscitation, intubation, stabilization, and ventilator management of premature infants in a clinical setting with the capacity to care for critically ill neonates. Infants should receive frequent clinical assessments so that oxygen and ventilator support can be modified to respond to changes in respiratory status. If administration-related adverse reactions such as bradycardia, oxygen desaturation, reflux of drug into the endotracheal tube (ETT), and airway/ETT obstruction should occur, dosing should be interrupted and the infant's clinical condition assessed and stabilized. Suctioning of the ETT or reintubation may be required if airway obstruction persists or is severe. After the patient is stable, dosing may proceed with appropriate monitoring. Adults with acute respiratory distress syndrome (ARDS) who received lucinactant via segmental bronchoscopic lavage had an increased incidence of death, multi-organ failure, sepsis, anoxic encephalopathy, renal failure, hypoxia, pneumothorax, hypotension, and pulmonary embolism. Lucinactant is not indicated for use in ARDS.

**Place in Therapy:** Lucinactant is the first non-animal derived surfactant containing a phospholipid and peptide composition. Lucinactant is under investigation for the treatment of meconium aspiration syndrome, acute respiratory distress syndrome, and the treatment and prevention of respiratory distress syndrome in the newborn.

**Notes:** Before use, warm the vial for 15 minutes in a preheated dry block heater at 44°C (111°F). After warming, shake the vial vigorously until the suspension is uniform and free-flowing. Record the date and time of warming in the space provided on the carton. If not used immediately after warming, lucinactant can be stored protected from light at room temperature for up to 2 hours. Do not return to the refrigerator after warming and discard within 2 hours. Vials are for single use only. Discard any unused portion. Each dose should be delivered in 4 aliquots. The first aliquot of the dose should be instilled as a bolus while continuing positive pressure mechanical ventilation and maintaining a positive end-expiratory pressure of 4 to 5 cm H2O.

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Peginesatide (Omontys®, Affymax Inc.)
Pharmacology: Erythropoiesis-stimulating agent (ESA).
Indication: Anemia due to chronic kidney disease in adult patients receiving dialysis.
Adverse Drug Reactions: Most commonly occurring adverse effects; dyspnea, diarrhea, nausea, cough, and arteriovenous fistula site complication.
Dose: 0.04mg/kg body weight administered once monthly.
Formulation: Single use vials-2mg/0.5mL, 3 mg/0.5mL, 4mg/0.5mL, 5mg/0.5mL, 6mg/0.5mL
Pre-filled syringes-1mg/0.5mL,2mg/0.5mL,3mg/0.5mL, 4mg/0.5mL, 5mg/0.5mL, 6mg/0.5mL
Multiple use vials-10mg/mL & 20mg/2mL
Warnings/Contraindications: There is an increased risk of mortality, myocardial infarction, stroke, and thromboembolism, thrombosis of vascular access and tumor progression or recurrence in patients who receive peginesatide. There is no evidence of added benefit when using ESAs to a target hemoglobin level > 11g/dL. Caution should be used when treating patients with peginesatide who have coexistent cardiovascular disease and stroke. Hypertension should be controlled before starting a patient on peginesatide. Hypertension should remain controlled throughout the treatment course.
Place in Therapy: Once monthly dosing may be advantageous over more frequent dosing regimens with other erythropoietin agents. When peginesatide once monthly and epoetin 1 to 3 times weekly were compared, it was found that other agents maintained hemoglobin levels in the prespecified range of 10 to 12 g/dL for 29 to 36 weeks in patients with CKD on dialysis who had previously been treated with epoetin alfa or epoetin beta. The proportion of patients with serious cardiovascular events was not significantly different with peginesatide compared with epoetin.
Notes: When converting from another ESA, peginesatide should be dosed once monthly based on the total weekly epoetin or darbepoetin alfa dose at the time of conversion. Patients taking peginesatide should contact their healthcare provider if they experience any new-onset neurologic symptoms or changes in seizure frequency. Peginesatide is not recommended nor indicated for patients with CKD not on dialysis, cancer patients receiving chemotherapy with anemia of non-renal etiology, and for patients requiring transfusions with RBC who need rapid correction of anemia.

Florbetapir F-18 (Amyvid®, Avid Radiopharms Inc)
Pharmacology: Radiopharmaceutical
Indication: Indicated as a diagnostic agent for positron emission tomography (PET) imaging of the brain to estimate b-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer’s Disease (AD) and other causes of cognitive decline.
Adverse Drug Reactions: Most commonly reported adverse reactions include headache, musculoskeletal pain, fatigue, and nausea.
Dose: Administer 370 MBq (10 mCi) as a single intravenous bolus in a total volume of 10 mL or less.
Formulation: Available as 10, 30, or 50 mL multidose vials of 500-1900 MBq/mL (13.5-51 mCi/mL).
Warnings/Contraindications: Florbetapir contributes to a patient’s long-term cumulative radiation exposure and risk.
Place in Therapy: Florbetapir does not establish a diagnosis of Alzheimer’s disease or other cognitive disorders, is not a predictor of development of dementia or other neurologic conditions, and should not be used to monitor response of therapies.
Notes: Florbetapir is a radioactive drug and should be handled with appropriate safety measures to minimize radiation exposure during administration. Drug interaction studies have not been extent to establish the extent, if any, to which concomitant medications may alter image results.

Avanafil (Stendra®, Vivus Inc)
Pharmacology: Phosphodiesterase type 5 enzyme inhibitor.
Indication: Indicated for the treatment of erectile dysfunction.
Adverse Drug Reactions: Most common adverse reactions (greater than or equal to 2%) include headache, flushing, nasal congestion, nasopharyngitis, and back pain.
Dose: The recommended starting dose is 100 mg approximately 30 minutes before sexual activity. Dose may be increased to a maximum dose of 200 mg or decreased to 50 mg.
Formulation: Available as 50-mg, 100-mg, or 200-mg tablets.
**Avanafil (Stendra®, Vivus Inc) continued**

**Warnings/Contraindications:** Concomitant use of nitrates in any form is contraindicated. Use with caution in patients with anatomical deformation of the penis or in those that may be predisposed to priapism. The use of avanafil is not recommended in patients with known hereditary degenerative retinal disorders, including retinitis pigmentosa. The safety of avanafil is unknown in patients with bleeding disorders and patients with active peptic ulceration.

**Place in Therapy:** Avanafil represents an alternative to other phosphodiesterase type 5 (PDE-5) inhibitors already available on the market. The selection of a specific PDE-5 inhibitor should be based on personal preferences, ease of use, cost of medication, and adverse effects profiles.

**Notes:** If alpha blocker therapy is indicated the dose of avanafil should be started at 50 mg of avanafil and should already be stable before starting avanafil. Do not use avanafil concomitantly with strong CYP3A4 inhibitor (including ketoconazole, ritonavir, azetanavir, clarithromycin, indinavir, itraconazole, nefazodone, nefinavir, saquinavir and telithromycin). In vitro studies with human platelets indicate that avanafil potentiates the anti-aggregatory effect of sodium nitroprusside.

**Taliglucerase Alfa (Elelyso®, Protalix LTD)**

**Pharmacology:** Lysosomal glucocerebrosidase-specific enzyme.

**Indication:** Long-term enzyme replacement therapy in adult patients diagnosed with Type-1 Gaucher disease.

**Adverse Drug Reactions:** Common adverse drug reactions occurring in ≥10% of patients include infusion reactions (44%); upper respiratory tract infections (22%); pharyngitis (19%); headache (19%); arthralgia (13%); and flu (13%).

**Dose:** The recommended dose of 60 units/kg of body weight every 2 weeks as an intravenous infusion for a minimum period of 60 minutes, up to 120 minutes. Initial rate of infusion should be 1.3 mL/min; rate can be increased to 2.3 mL/min dependent upon patient tolerability. Dose can be adjusted based on patient’s therapeutic response; doses ranging from 11 units/kg to 73 units/kg have been evaluated in clinical studies; however, data pertaining to overdose is not available.

**Formulation:** 200 units/vial lyophilized powder for reconstitution.

**Reconstitution:** Prior to reconstitution, vials must be stored in the refrigerator (2 to 8°C or 36 to 46°F). Calculate patient-specific dose and round up to next whole vial. Reconstitute each vial with 5.1 mL of sterile water for injection (SWFI); yields final volume of 5.3 mL. Gently mix vials (DO NOT SHAKE); solution should appear clear and colorless with no particulate matter. Withdraw 5 mL of reconstituted solution from each vial being used and dilute with 0.9% Sodium Chloride Injection to a final volume of 100-200 mL (slight flocculation may occur after dilution due to the proteinaceous nature of the product).

**Warnings/Contraindications:** No contraindications stated by the manufacturer. Precautions are warranted regarding potential anaphylaxis and allergic/infusion reactions. Anaphylaxis was observed in clinical studies and taliglucerase alfa should be discontinued immediately if anaphylaxis occurs. Allergic/infusion reactions, defined by reactions occurring within 24 hours of receipt of infusion, accounted for 44% of adverse drug reactions in clinical studies. The most common infusion reaction symptoms include headache, urticaria, flushing, and erythema. Slowing the infusion rate or treating with antihistamines and antipyretics may be beneficial in managing the occurrence of infusion reactions.

**Place in Therapy:** The safety and efficacy of taliglucerase alfa was assessed in 25 patients with Type 1 Gaucher disease who were switched from imiglucerase to taliglucerase alfa. Patients were able to maintained stable organ volume and hematologic values after switching therapies to taliglucerase alfa.

**Note:** Safety and efficacy have not been established in pediatric patients; geriatric patients (>65 years of age) accounted for a small representation in clinical studies and data is insufficient to determine if response would be substantially different compared to younger adults.

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**Lorcaserin HCl (Belviq®, Arena Pharms)**

**Pharmacology:** Serotonin type 2C (5-HT2C) receptor agonist.

**Indication:** Indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) 30 kg/m² or greater or 27 kg/m² or greater in the presence of at least one weight-related comorbid condition.

**Adverse Drug Reactions:** Most common adverse reactions (greater than 5%) are headache, dizziness, fatigue, nausea, dry mouth, and constipation, and in diabetic patients are hypoglycemia, headache, back pain, cough, and fatigue.

**Dose:** 10 mg twice daily.

**Formulation:** 10 mg film-coated tablets.

**Warnings/Contraindications:** The safety of coadministration with other serotonergic or antidopaminergic agents has not been established. Manage with immediate discontinuation and provide supportive treatment if Serotonin Syndrome or Neuroleptic Malignant Syndrome (NMS) is suspected. If signs or symptoms of valvular heart disease develop consider discontinuation and evaluate the patient for possible valvulopathy. Monitor for depression or suicidal thoughts. Patients should seek emergency treatment if an erection lasts >4 hours. Use lorcaserin with caution in patients predisposed to priapism.

**Place in Therapy:** Represents a novel mechanism of action in the treatment of obesity.

**Notes:** Discontinue if 5% weight loss is not achieved by week 12.

**Mirabegron (Myrbetriq®, Astellas)**

**Pharmacology:** Beta-3 adrenergic receptor agonist.

**Indication:** Indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

**Adverse Drug Reactions:** Most commonly reported adverse reactions were hypertension, nasopharyngitis, urinary tract infection and headache.

**Dose:** Recommended starting dose is 25 mg once daily, with or without food, may increase dose to 50 mg once daily. 

**Severe Renal Impairment or Moderate Hepatic Impairment:** Maximum dose is 25 mg once daily.

**Patients with End Stage Renal Disease (ESRD) or Patients with Severe Hepatic Impairment:** Not recommended

**Formulation:** Available as 25-mg and 50-mg extended release tablets.

**Warnings/Contraindications:** Mirabegron is not recommended for use in severe uncontrolled hypertensive patients. Concomitant administration with antimuscarinic drugs should be done so with caution because of risk of urinary retention.

**Place in Therapy:** Represents a new approach to treating overactive bladder. In three randomized, double-blind, parallel-group, multicenter, 12-week studies, the daily mean number of micturitions and incontinence episodes and volume voided per micturition significantly improved with the use of mirabegron compared with placebo.

**Notes:** Mirabegron is a moderate inhibitor of CYP2D6.
### NEW BIOLOGIC APPROVALS OF 2012
(Click on generic drug name for further information)

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### Glucarpidase (Voraxaze, BTG International Inc)
**Pharmacology:** Glucarpidase converts methotrexate to its inactive metabolites, providing an alternative non-renal pathway for methotrexate elimination.

**Indication:** Indicated for the treatment of toxic plasma methotrexate concentrations (>1 µmol/L) in patients with delayed methotrexate clearance due to impaired renal function.

**Adverse Drug Reactions:** Occurring in >1% of patients: paraesthesia, flushing, nausea and/or vomiting, hypotension and headache.

**Dose:** 50 Units per kg as a single intravenous injection.

**Formulation:** 1,000 Units/vial lyophilized powder

**Warnings/Contraindications:** Serious allergic reactions, including anaphylactic reactions, may occur. Do not administer leucovorin within 2 hours before or after a dose of glucarpidase. For 48 hours after glucarpidase administration, determine the leucovorin dose based on the patient’s pre-glucarpidase methotrexate concentration. Glucarpidase is not indicated for use in patients who exhibit the expected clearance of methotrexate (plasma methotrexate concentrations within 2 standard deviations of the mean methotrexate excretion curve specific for the dose of methotrexate administered) or those with normal or mildly impaired renal function because of the potential risk of subtherapeutic exposure to methotrexate.

**Place in Therapy:** In a case series of 100 patients (median age, 17 years; range, 0.3 to 82 years) experiencing high-dose methotrexate-induced nephrotoxicity, glucarpidase was associated with reduced serum methotrexate levels and normalization of renal function. These benefits were attenuated, however, when glucarpidase was given more than 96 hours after methotrexate administration.

**Notes:** Potential exogenous substrates of glucarpidase include reduced folates, folate antimetabolites, and leucovorin. Measurement of methotrexate using immunoassays is unreliable for samples collected within 48 hours following glucarpidase administration. Continue therapy with leucovorin until the methotrexate concentration has been maintained below the leucovorin treatment threshold for a minimum of three days.

### Pertuzumab (Perjeta®, Genentech)
**Pharmacology:** Antineoplastic Agent, Anti-Human Epidermal Growth Factor Receptor type 2 (HER2); Antineoplastic Agent, Monoclonal Antibody.

**Indication:** Indicated in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

**Adverse Drug Reactions:** Most common (> 30%) in combination with trastuzumab and docetaxel were diarrhea, alopecia, neutropenia, nausea, fatigue, rash, and peripheral neuropathy.

**Dose:** The initial dose is 840 mg administered as a 60-minute intravenous infusion, followed every 3 weeks thereafter by 420 mg administered as a 30 to 60 minute intravenous infusion.

**Formulation:** 420 mg/14 mL single-use vial.

**Warnings/Contraindications:** No contraindications listed. Fetal harm can occur when administered to a pregnant woman. Monitor LVEF and withhold dosing as appropriate. Infusion-associated Reactions, Hypersensitivity Reactions/Anaphylaxis have been associated with pertuzumab administration. If a significant infusion-associated reaction occurs, slow or interrupt the infusion and administer appropriate medical therapies.
**Pertuzumab (Perjeta®, Genentech) continued**

**Place in Therapy:** In the randomized, double-blind, phase three CLEOPATRA trial (n=808) pertuzumab in combination with trastuzumab and docetaxel significantly extended progression-free survival by 6.1 months compared with placebo plus trastuzumab and docetaxel.

**Notes:** For intravenous infusion only. Do not administer as an intravenous push or bolus.

**Meningococcal Groups C, Y and Haemophilus b Tetanus Toxoid Conjugate Vaccine (MenHiBrix®, GlaxoSmithKline)**

**Pharmacology:** Vaccine.

**Indication:** Active immunization to prevent invasive disease caused by Neisseria meningitidis serogroups C and Y and *Haemophilus influenzae* type b; but is not a substitute for routine tetanus immunization. The agent is approved for use in children 6 weeks through 18 months of age.

**Adverse Drug Reactions:** Rates of local injection site pain, redness, and swelling ranged from 15% to 46% depending on reaction and specific dose in schedule. Commonly reported systemic events included irritability (62% to 71%), drowsiness (49% to 63%), loss of appetite (30% to 34%), and fever (11% to 26%) (specific rate depended on the event and dose in the schedule).

**Dose:** Four doses by intramuscular injection at 2, 4, 6, and 12 through 15 months of age. The first dose may be given as early as 6 weeks. The fourth dose may be given as late as 18 months of age.

**Formulation:** Solution for injection supplied as a single-dose vial of lyophilized vaccine to be reconstituted with the accompanying vial of saline diluent. A single dose after reconstitution is 0.5 mL.

**Warnings/Contraindications:** Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any meningococcal-, H. influenzae type b-, or tetanus toxoid-containing vaccine or any component of MenHiBrix. If Guillain-Barré syndrome has occurred within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including MenHiBrix, should be based on consideration of the potential benefits and possible risks. Syncope (fainting) can occur in association with administration of injectable vaccines, including MenHiBrix. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope. Apnea following intramuscular vaccination has been observed in some infants born prematurely. Decisions about when to administer an intramuscular vaccine, including MenHiBrix, to infants born prematurely should be based on consideration of the individual infant’s medical status, and the potential benefits and possible risks of vaccination.

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Fentanyl Sublingual Spray (Subsys®, Insys Therap)
Pharmacology: Opioid agonist.
Indication: Management of breakthrough pain in adult cancer patients who are already receiving and are tolerant to opioid therapy for persistent cancer pain. Patients must remain on continuous opioid therapy when receiving fentanyl sublingual spray.
Dosage form: 100 mcg, 200 mcg, 400 mcg, 600 mcg, and 800 mcg sublingual spray.
Dose: Initial dose is 100 mcg per episode of breakthrough pain. Titrate to a tolerable dose that provides adequate analgesia to treat breakthrough pain. No more than 2 doses should be used for each episode of breakthrough pain. Wait at least 4 hours before treating another episode of breakthrough pain. Dosage should be limited to ≤ 4 doses per day.
Place in Therapy: Alternative to other sublingual opioids for breakthrough pain.

Tenofovir Disoproxil Fumarate Oral Powder (Viread®, Gilead Sciences Inc)
Pharmacology: Nucleotide analog HIV-1 reverse transcriptase inhibitor and HBV reverse transcriptase inhibitor.
Indication: Adjunctive treatment of HIV-1 infection in patient’s ≥ 2 years when used with other antiretroviral agents; treatment of chronic hepatitis B in adults.
Dosage form: 40 mg per 1 g of oral powder.
Dose: Adults: 300 mg orally once daily with or without food; CrCl: 30-49 mL/min: 300 mg every 48 hours; CrCl: 10-29 mL/min: 300 mg every 72 to 96 hours; Hemodialysis: 300 mg every 7 days or after approximately 12 hr of dialysis.
Pediatrics (Ages 2-18): Oral powder-8 mg/kg once daily with food (max of 300 mg/day); tablets- 8 mg/kg once daily (150 mg, 200 mg, 250 mg, or 300 mg) with or without food. Patients must weigh at least 17 kg to take tablets.
Place in Therapy: Adjunctive treatment of HIV-1 infection in patient’s ≥ 2 years.

Ciclesonide Nasal Aerosol (Zetonna®, Nycomed Gmbh)
Pharmacology: Nasal Corticosteroid
Indication: Symptoms associated with seasonal and perennial allergic rhinitis in patients 12 years of and older.
Dosage form: Nasal aerosol (6.1 g canister containing 60 actuations; 37 mcg per actuation).
Dose: 1 spray (37 mcg) per nostril once daily
Place in Therapy: Alternative to other commercially available nasal corticosteroids.

Exenatide Extended Release (Bydureon, Amylin)
Pharmacology: Glucagon-like peptide-1 receptor agonist.
Indication: Adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
Dosage form: Extended-release injectable suspension (2 mg).
Dose: 2 mg subcutaneously once weekly with or without food. Administer immediately after the powder is suspended.
Place in Therapy: In the DURATION-1 trial it was found that patient who switched from exenatide twice daily to exenatide weekly after 30 weeks experienced further improvements in hemoglobin A1C (HbA1c) and Fasting Plasma Glucose (FPG) with sustained weight loss. Patients taking exenatide weekly experienced nausea less frequently and was predominantly mild.

Linagliptin/Metformin (Jentadueto®, Boehringer Ingelheim Pharmaceuticals Inc)
Pharmacology: Dipeptidyl peptidase-4 (DPP-IV) inhibitor and oral biguanide combination
Indication: Type 2 diabetes mellitus in combination with diet and exercise.
Dosage form: Tablets (2.5mg/500mg; 2.5mg/850mg; 2.5mg/1000mg).
Dose: Linagliptin/metformin combination therapy is to be administered by mouth twice a day with specific dose individualized based on efficacy and tolerability. In patients currently not treated with metformin, initiate treatment with linagliptin 2.5mg / metformin 500mg by mouth twice daily with meals. In patients currently treated with metformin, initiate at the dose the patient is currently taking at two daily meals. Maximum dosage limits are 5mg of linagliptin and 2000mg of metformin.

(Back to New Drug Formulations/Combinations table)
**Linagliptin/Metformin (Jentadueto®, Boehringer Ingelheim Pharmaceuticals Inc) continued**

**Place in Therapy:** Linagliptin/metformin hydrochloride is approved as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes mellitus when treatment with both linagliptin and metformin is appropriate. In a clinical trial enrolling patients with type 2 diabetes patients inadequately controlled with diet and exercise, initiating combination therapy with linagliptin/metformin was associated with HbA1c reduction ranging from 1.2% to 1.6%, whereas in clinical trials enrolling patients with type 2 diabetes patients inadequately controlled with previous oral therapy, adding linagliptin to metformin, or to the combination of a sulfonylurea and metformin, was associated with HbA1c reduction ranging from 0.4% to 0.7%.

**Sitagliptan/Metformin XR (Janumet XR®, Merck Sharp & Dohme Corp)**

**Pharmacology:** Dipeptidyl peptidase-4 (DPP-IV) inhibitor and oral biguanide combination.

**Indication:** Type 2 diabetes mellitus uncontrolled by diet and exercise and when treatment with one anti-diabetic agent alone does not achieve adequate control.

**Dosage form:** Tablets (50mg/500mg; 50mg/1000mg; 100/1000mg).

**Dose:** In patients previously taking metformin immediate release 850-1000 mg twice daily, the starting dose is two 50mg sitagliptan/1000mg metformin extended release tablets PO once daily with a meal, preferably in the evening. For use when sitagliptan alone does not provide adequate glycemic control, the usual starting dose is sitagliptan 100mg/metformin 1000mg PO once daily with a meal. Maximum dosage limits are sitagliptan 100mg/day and metformin 2000mg/day. Doses are to be individualized based on efficacy and tolerability.

**Place in Therapy:** Due to the lack of long-term safety and effectiveness studies, and comparative data, the place of this combination relative to other anti-diabetic modalities cannot be adequately assessed. There have been no clinical efficacy or safety studies conducted with metformin/sitagliptan XR to characterize its effect on HbA1c reduction.

**Balsalazide Disodium (Giazo®, Nexgen Pharma, Inc)**

**Pharmacology:** Locally acting aminosalicylate

**Indication:** Treatment of mild to moderately active ulcerative colitis in males 18 years of age and older.

**Dosage form:** Available as 1.1 gram tablet

**Dose:** Patients should take three 1.1g tablets PO twice a day with or without food up to 8 weeks.

**Place in Therapy:** Balsalazide disodium tablets 3.3 g twice daily, demonstrated a significant clinical improvement in men compared with placebo, but not in women and efficacy had not been established beyond 8 weeks of therapy.

**Mitomycin Topical Solution (Mitosol®, Mobius Therapeutics LLC)**

**Pharmacology:** Antineoplastic Agent; Antimetabolite

**Indication:** Adjunct to ab externo glaucoma surgery.

**Dosage form:** Mitomycin topical solution is a sterile lyophilized mixture of mitomycin and mannitol, which, when reconstituted with sterile water for injection, provides a solution for application in glaucoma filtration surgery. It is supplied in vials containing 0.2 mg of mitomycin. Each vial also contains mannitol 0.4 mg, in a 1:2 ratio of mitomycin to mannitol. Each milliliter of reconstituted solution contains 0.2 mg mitomycin and has a pH between 5.0 and 8.0.

**Dose:** Mitomycin topical solution is intended for topical application to the surgical site of glaucoma filtration surgery; it is not intended for intraocular administration. Sponges provided with the mitomycin topical solution kit should be fully saturated with entire reconstituted contents and then applied to a treatment area approximating 10mm/6mm, +/- 2mm. Sponges are to be applied in a single layer, utilizing surgical forceps. Sponges are to remain on treatment area for two minutes, then removed, and disposed of properly with other chemotherapy waste.

**Place in Therapy:** This formulation allows for easy administration to the surgical site during glaucoma filtration surgery.
Ivermectin Lotion (Sklice®, Sanofi Pasteur, Inc)
Pharmacology: Pediculicide.
Indication: Topical treatment of head lice in patients 6 months of age and older.
Dosage form: 0.5% lotion.
Dose: Apply lotion to dry hair in amount sufficient (up to 1 tube) to thoroughly coat the hair and scalp.
Leave lotion on the hair and scalp for 10 minutes, and then rinse off with water. The tube is intended for single use; discard any unused portion.
Place in Therapy: Two multicenter randomized, double-blind, placebo-controlled studies were performed to elucidate the effectiveness of a single 10 minute treatment with ivermectin 0.5% topical lotion compared to placebo. It was found that ivermectin 0.5% lotion was associated with a higher proportion of lice free patients compared to placebo.

Alendronate Sodium Effervescent Tablet (Binosto®, Effrx Pharm. SA)
Pharmacology: Bisphosphonate.
Indication: For the treatment of osteoporosis in postmenopausal women, and as a treatment to increase bone mass in men with osteoporosis.
Dosage form: 70mg Strawberry-flavored effervescent tablet.
Dose: 70mg tablet once weekly dissolved in 4 ounces of plain room temperature water.
Place in Therapy: Currently commercially unavailable as of July 18, 2012.

Beclomethasone Dipropionate Aerosol Spray (Qnasl®, Teva)
Pharmacology: Nasal Corticosteroid.
Indication: For the treatment of nasal symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescents 12 years of age and older.
Dosage form: Nasal aerosol.
Dose: 2 (320 mcg) sprays in each nostril once daily (maximum 4 sprays per day).
Place in Therapy: Beclomethasone dipropionate aerosol spray offers once daily dosing compared to alternative beclomethasone dipropionate dosage forms currently available on the market.

Phentermine ODT (Suprenza®, Citius Pharms)
Pharmacology: Sympathomimetic amine anorectic.
Indication: As a short-term adjunct (a few weeks) in a regimen of weight reduction based on exercise, behavioral modification and caloric restriction in the management of exogenous obesity for patients with an initial body mass index greater than or equal to 30kg/m², or greater than or equal to 27kg/m² in the presence of other risk factors (e.g. controlled hypertension, diabetes, hyperlipidemia).
Dosage form: Orally-disintegrating tablets (15mg, 30mg).
Dose: Dosage should be individualized to obtain an adequate response with the lowest effective dose.
Place in Therapy: Phentermine ODT represents an alternative to currently available dosage forms.
There have been no clinical studies performed on phentermine ODT.

Azelastine Hydrochloride/Fluticasone Propionate (Dymista®, Meda Pharms)
Pharmacology: Second-generation anti-histamine and nasal corticosteroid.
Indication: Symptomatic relief of seasonal allergic rhinitis in patients 12 years of age and older who require treatment with both active ingredients.
Adverse Drug Reactions: Common reactions occurring ≥2% include dysgeusia; headache; and epistaxis.
Dose: One spray per nostril twice daily.
Formulation: Nasal spray suspension; 137 mcg of azelastine and 50 mcg of fluticasone per spray.
Warnings/Contraindications: No contraindications stated by the manufacturer. Warnings and precautions include; somnolence (decreased alertness); local nasal effects (i.e., epistaxis); glaucoma/cataracts (due to possible increase in intraocular pressure); immunosuppression (possible increased risk of infection with steroid use); Hypothalamic-Pituitary-Adrenal (HPA) Axis effects (i.e., hypercorticism and adrenal suppression); concurrent use with CYP 3A4 inhibitors (i.e., ritonavir known to increase serum fluticasone levels); and effects on growth (pediatric patients may experience reduced growth velocity).

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Place in Therapy: Clinical studies have demonstrated superior control of symptoms such as rhinorrhea, sneezing, and nasal pruritus when compared with placebo, and when compared with either azelastine or fluticasone monotherapy.

Note: Safety and efficacy have not been established in pediatric patients less than 12 years of age. The product is for nasal use only; avoid contact with eyes and mouth. If spray comes into contact with eyes, immediately flush eyes with plenty of water. Avoid tilting head back while administering nasal spray to mitigate potential drainage into the throat; medication has a bitter taste. Azelastine/fluticasone nasal spray should be stored at controlled room temperature; do not refrigerate or freeze.

Tazarotene Topical Foam (Fabior®, Stiefel Labs)
Pharmacology: Keratolytic
Indication: Topical retinoid treatment for acne vulgaris in patients 12 years of age and older.
Adverse Drug Reactions: Common adverse drug reactions occurring in ≥6% of patients are related to the application site and include irritation (14%); dryness (7%); erythema (6%); and exfoliation (6%).
Dose: Dispense a small amount of foam into the palm of hand and apply a thin layer to the affected areas of the face and/or upper trunk once daily in the evening. Massage foam into skin until it disappears; avoid contact with eyes, lips, and mucous membranes.
Formulation: 0.1% foam.
Warnings/Contraindications: Contraindicated in pregnancy; topical or systemic retinoid administration has been associated with teratogenic effects in both rats and rabbits. Warnings and precautions are associated with the use of this product. Systemic exposure may induce fetal risk; topical application to a sufficient body surface area may mimic systemic exposure in animal models; however, it is unknown what level of exposure induces teratogenicity. Local irritation is common and individuals may experience skin redness, peeling, or burning. Discontinuation or reduced frequency of product usage is recommended in the event skin irritation occurs. Use caution when applying concomitant acne formulations; irritation effects may become exacerbated. Retinoid products are known photosensitizing agents; avoid sun exposure (including sunlamps) and apply sunscreen if daily activities require prolonged sun exposure. Avoid open flames and smoking after application of the foam due to the flammable propellant used in the product.
Place in Therapy: Tazarotene topical foam represents an alternative to current commercially available creams and gels.
Note: Safety and efficacy have not been established in pediatric patients less than 12 years of age. It is recommended to apply the product in the evening after washing with a mild cleanser and completely drying the affected area. This product should not be applied to abraded or eczematous skin, or severe irritation may occur. Product should be stored upright at controlled room temperature.

Isotretinoin (Absorica®, Cipher Pharm Inc)
Pharmacology: Retinoid agent.
Indication: For the treatment of severe recalcitrant nodular acne in patients 12 years of age and older.
Dosage form: Capsules - 10 mg, 20 mg, 30 mg and 40 mg.
Dose: Recommended dose - 0.5 to 1 mg/kg/day given in two divided doses for 15 to 20 weeks; once daily dosing is not recommended.
Notes: The medication is only to be given to patients that are registered for the iPLEDGE program. Patients are to be counseled on proper sexual precautions. Pregnancy tests are to be completed previous to prescribing, each month during therapy, end of therapy, and one month after discontinuation of therapy. A fasting lipid profile and liver function tests should be performed also prior to prescribing.
Place in Therapy: This product adds to the current treatment options available for severe recalcitrant nodular acne.

Cefixime Capsule (Suprax®, Lupin Ltd)
Pharmacology: 3rd Generation Cephalosporin Antibiotic.
Indication: To treat uncomplicated urinary tract infections, otitis media, pharyngitis, tonsillitis, acute issues of chronic bronchitis, uncomplicated cervical or urethral gonorrhea
Dosage form: Capsules: 400 mg
**Dose:** Adults: 400 mg daily; Children: 8 mg/kg/day (weight-based dosing and reconstitution instructions are located in the package insert)

**Place in Therapy:** This formulation may be advantageous for patients who prefer a capsular dosage form.

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# New Drug Indications of 2012

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### Pazopanib (Votrient®, Glaxosmithkline)

**Pharmacology:** Tyrosine kinase inhibitor.

**Indication:** Treatment of patients with advanced soft tissue sarcoma (STS) who have received prior chemotherapy.

**Dose:** 800 mg once daily.

### Insulin Detemir (Levemir®, Novo Nordisk)

**Pharmacology:** Recombinant insulin.

**Indication:** Treatment for Type 1 diabetes in children ages 2 to 5 years old.

**Dose:** Approximately one-third of the total daily insulin requirement; a rapid-acting or short-acting insulin should also be used. If administered once daily, doses are generally administered with evening meals or at bedtime.

### Immune Globulin Infusion (Gammagard Liquid®, Baxter)

**Pharmacology:** Opsonizing and neutralizing IgG antibodies agonist.

**Indication:** Maintenance for multifocal motor neuropathy (MMN).

**Dose:** 0.5 to 2.4 grams/kg/month based on clinical response.

### Pregabalin (Lyrica®, Pfizer)

**Pharmacology:** Anticonvulsant.

**Indication:** Management of neuropathic pain associated with spinal cord injury.

**Dose:** Maximum initial dose in 300 mg/day split into two divided doses per day, may increase to a maximum dose of 600 mg/day.

References available on file.