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DRUG DISCOVERY

FDA approved drugs - August 2012

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1. LUCENTIS (RANIBIZUMAB INJECTION)

1.1. Company

Genentech; Approved August 2012

1.2. Treatment area

Diabetic macular edema

1.3. General Information

Lucentis (ranibizumab) is a therapeutic antibody fragment designed to inhibit vascular endothelial growth factor A (VEGF-A), a protein that plays a critical role in ocular angiogenesis. Blocking VEGF-A can decrease abnormal new blood vessel formation and the resultant leaking of serum into the retina. It is specifically indicated for diabetic macular edema. It is supplied as a solution for intravitreal injection. The recommended dose of Lucentis for diabetic macular edema is 0.3 mg (0.05 mL of 6 mg/mL solution) administered once a month (approximately 28 days).

1.4. Mechanism of Action

Lucentis (ranibizumab) is a recombinant humanized IgG1 kappa isotype monoclonal antibody fragment designed for intraocular use. Ranibizumab binds to and inhibits the biologic activity of human vascular endothelial growth factor A (VEGF-A). VEGF-A has been shown to cause neovascularization and leakage in models of ocular angiogenesis and vascular occlusion and is thought to contribute to pathophysiology of neovascular AMD, macular edema following RVO, and DME. The binding of ranibizumab to VEGF-A prevents the interaction of VEGF-A with its receptors (VEGFR1 and VEGFR2) on the surface of endothelial cells, reducing endothelial cell proliferation, vascular leakage, and new blood vessel formation.

1.5. Side Effects

Adverse events associated with the use of Lucentis for diabetic macular edema may include, but are not limited to, the following: conjunctival hemorrhage, eye pain, vitreous floaters, increased IOP, increased redness in the white of the eye, eye pain, small specks in vision, and increased eye pressure. The most common non–eye-related side effects are nose and throat infections, headache, lung/airway infections, and nausea.

2. LINZESS (LINACLOTIDE)

2.1. Company

Forest Labs and Ironwood Pharmaceuticals; Approved August 2012

2.2. Treatment Area

Irritable bowel syndrome with constipation and chronic idiopathic constipation

2.3. General Information

Linzess (linaclotide) is a guanylate cyclase-C (GC-C) agonist. It is specifically indicated for the treatment of adults with irritable bowel syndrome with constipation and for adults with chronic idiopathic constipation. It is supplied as a tablet for oral administration. The recommended dose of Linzess for irritable bowel syndrome with constipation is 290 mcg taken orally once daily on an empty stomach, at least 30 minutes prior to the first meal of the day. The recommended dose of Linzess for chronic idiopathic constipation is 145 mcg taken orally once daily on an empty stomach, at least 30 minutes prior to the first meal of the day.

2.4. Mechanism of Action

Linaclotide and its active metabolite bind to GC-C and act locally on the luminal surface of the intestinal epithelium. Activation of GC-C results in an increase in both intracellular and extracellular concentrations of cyclic guanosine monophosphate (cGMP). Elevation in intracellular cGMP stimulates secretion of chloride and bicarbonate into the intestinal lumen, mainly through activation of the cystic fibrosis transmembrane conductance regulator (CFTR) ion channel, resulting in increased intestinal fluid and accelerated transit.

2.5. Side Effects

Adverse reactions associated with the use of Linzess may include, but are not limited to, the following: diarrhea, abdominal pain, flatulence, abdominal distension.

3. ZALTRAP (ZIV-AFLIBERCEPT)

3.1. Company

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Sanofi Aventis US; Approved August 2012

3.2. Treatment Area
Metastatic colorectal cancer

3.3. General Information
Zaltrap (ziv-aflibercept) is a fusion protein specifically designed to bind all forms of Vascular Endothelial Growth Factor-A (VEGF-A) and Placental Growth Factor (PlGF). Both VEGF-A and PlGF are proteins that are involved in the abnormal growth of new blood vessels. Zaltrap is specifically approved in combination with 5-fluorouracil, leucovorin, irinotecan-(FOLFIRI) for patients with metastatic colorectal cancer that is resistant to or has progressed following an oxaliplatin-containing regimen. It is supplied as an injection for intravenous infusion. The recommended dose is 4 mg per kg over one hour every two weeks. It should be continued until disease progression or unacceptable toxicity.

3.4. Mechanism of Action
Ziv-aflibercept is a recombinant fusion protein consisting of Vascular Endothelial Growth Factor (VEGF)-binding portions from the extracellular domains of human VEGF Receptors 1 and 2 fused to the Fc portion of the human IgG1. By binding to these endogenous ligands, ziv -aflibercept can inhibit the binding and activation of their cognate receptors. This inhibition can result in decreased neovascularization and decreased vascular permeability. Ziv-aflibercept is produced by recombinant DNA technology in a Chinese hamster ovary (CHO) K-1 mammalian expression system.

3.5. Side Effects
Adverse events associated with the use of Zaltrap for colorectal cancer may include, but are not limited to, the following: leucopenia, diarrhea, neutropenia, proteinuria, AST increased, stomatitis, fatigue, thrombocytopenia, ALT increased, hypertension, weight decreased, decreased appetite, epistaxis, abdominal pain, dysphonia, serum creatinine increased, headache.

4. XTANDI (ENZALUTAMIDE)
4.1. Company
Medivation; Approved August 2012

4.2. Treatment Area
Metastatic castration-resistant prostate cancer

4.3. General Information
Xtandi (enzalutamide) is an androgen receptor inhibitor. It is specifically indicated for the treatment of patients with metastatic castration-resistant prostate cancer who have previously received docetaxel. It is supplied as a capsule for oral administration. The recommended dose of Xtandi is 160 mg (four 40 mg capsules) administered orally once daily. It can be taken with or without food. The capsules should be swallowed whole.

4.4. Mechanism of Action
Xtandi (enzalutamide) acts on different steps in the androgen receptor signaling pathway. Enzalutamide has been shown to competitively inhibit androgen binding to androgen receptors and inhibit androgen receptor nuclear translocation and interaction with DNA.

4.5. Side Effects
Adverse events associated with the use of Xtandi may include, but are not limited to, the following: 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, paraesthesia, anxiety, hypertension.

5. MARQIBO (VINCRISTINE SULFATE LIPOSOMES) INJECTION
5.1. Company
Talon Therapeutics Inc.; Approved August 2012

5.2. Treatment Area
Acute Lymphoblastic Leukemia

5.3. General Information
Marqibo (vincristine sulfate liposome injection) is a vinca alkaloid indicated for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL). Marqibo is a novel, sphingomyelin/cholesterol liposome-encapsulated, formulation of vincristine sulfate. Vincristine, a microtubule inhibitor, is FDA-approved for ALL and Non-Hodgkin's Lymphoma (NHL) and is widely used in combination regimens for treatment for a variety of adult and pediatric hematologic and solid tumor malignancies.

5.4. Mechanism of Action
Vincristine sulfate, the active agent in Marqibo, is also a substrate for P glycoprotein (P gp). The effect of concomitant use of potent P gp inhibitors or inducers has not been investigated; it is likely that these agents will alter the pharmacokinetics or pharmacodynamics of Marqibo. Therefore the concomitant use of potent P gp inhibitors or inducers should be avoided.

5.5. Side Effects
Adverse events associated with the use of Marqibo may include, but are not limited to, the following: Nausea, fever, diarrhea, decreased appetite, sleep problems, fatigue, and nerve problems.

6. AUVI-Q (EPINEPHRINE) INJECTION
6.1. Company
Sanofi; Approved August 2012

6.2. Treatment Area
Anaphylaxis, Allergic Reaction

6.3. General Information
Auvi-Q (epinephrine injection) is a voice-guided epinephrine auto-injector for the emergency treatment of life-threatening allergic reactions in people who are at risk for or have a history of anaphylaxis. It is available in two different dosages, Auvi-Q 0.3mg delivers 0.3mg epinephrine injection and is intended for patients who weigh 66 pounds or more. Auvi-Q 0.15mg delivers 0.15mg epinephrine injection and is intended for patients who weigh 33 – 66 pounds.

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Auvi-Q has not been studied in patients weighing less than 33 pounds. Each Auvi-Q pack contains two devices - containing one dose of epinephrine each - and a non-active training device.

6.4. Mechanism of Action

Auvi-Q (epinephrine injection) is used to treat life-threatening allergic reactions (anaphylaxis) in people who are at risk for or have a history of these reactions. It is the size and shape of a credit card, the thickness of a cell phone and fits comfortably in a pocket or small purse. During a life-threatening allergic reaction, Auvi-Q talks the user through each step of the injection process. If the patient or caregiver needs more time, it repeats the step-by-step directions. An anaphylactic reaction is a life-threatening allergic reaction that can happen within minutes and can be caused by stinging and biting insects (bees, wasps, hornets, and mosquitoes), allergy shots, foods, medicines, exercise, or other unknown causes.

6.5. Side Effects

The most common side effects may include increase in heart rate, stronger or irregular heartbeat, sweating, nausea and vomiting, difficulty breathing, paleness, dizziness, weakness or shakiness, headache, apprehension, nervousness, or anxiety.

7. STRIBILD (COBICISTAT, ELVITEGRAVIR, EMTRICITABINE AND TENOFOVIR) TABLETS

7.1. Company

Gilead Sciences, Inc.; Approved August 2012

7.2. Treatment Area

HIV Infection

7.3. General Information

Stribild (cobicistat, elvitegravir, emtricitabine and tenofovir) is a complete once-daily single tablet regimen for HIV-1 infection for treatment-naïve adults. Elvitegravir is a member of the integrase inhibitor class of antiretroviral compounds. Integrase inhibitors interfere with HIV replication by blocking the ability of the virus to integrate into the genetic material of human cells. Stribild contains four compounds in a complete once-daily, single tablet regimen: elvitegravir 150 mg; cobicistat 150 mg; emtricitabine 200 mg; and tenofovir disoproxil fumarate 300 mg. Stribild is indicated as a complete regimen for the treatment of HIV-1 infection in adults who are antiretroviral treatment-naïve. Stribild does not cure HIV-1 infection. Adult dosage: One tablet taken orally once daily with food.

7.4. Mechanism of Action

Stribild can alter the concentration of drugs metabolized by CYP3A or CYP2D6. Do not use with drugs highly dependent on these factors for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening adverse events. Drugs that induce CYP3A can decrease the concentrations of components of Stribild. Do not use with drugs that strongly induce CYP3A as this may lead to loss of virologic response and possible resistance to Stribild.

7.5. Side Effects

The most common side effects may includes: feel very weak or tired, have unusual (not normal) muscle pain, have trouble breathing, have stomach pain with, nausea, vomiting, feel cold, especially in your arms and legs, feel dizzy or lightheaded, have a fast or irregular heartbeat.

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