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DRUG DISCOVERY

FDA approved drugs – May 2013

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1. LIPTRUZET (EZETIMIBE AND ATORVASTATIN)

1.1. Company

Merck; Approved by May 2013

1.2. Treatment Area

Hyperlipidemia

1.3. General Information

Liptruzet (ezetimibe and atorvastatin) treats two sources of cholesterol by inhibiting both the absorption of cholesterol in the digestive tract - through ezetimibe - and the production of cholesterol in the liver - through atorvastatin. It is specifically indicated for the reduction of elevated total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), apolipoprotein B (Apo B), triglycerides (TG), and non-high-density lipoprotein cholesterol (non-HDL-C), and to increase high-density lipoprotein cholesterol (HDL-C) in patients with primary (heterozygous familial and non-familial) hyperlipidemia or mixed hyperlipidemia. It is also indicated for the reduction of elevated total-C and LDL-C in patients with homozygous familial hypercholesterolemia, as an adjunct to other lipid-lowering treatments (e.g., LDL apheresis) or if such treatments are unavailable. It is supplied as a tablet for oral administration. The recommended dose range is 10/10 mg/day to 10/80 mg/day. The recommended starting dose of Liptruzet is 10/10 mg/day or 10/20 mg/day. It can be administered as a single dose at any time of the day, with or without food. The recommended starting dose for patients who require a larger reduction in LDL-C (greater than 55%) is 10/40 mg/day. After initiation and/or upon titration of Liptruzet, lipid levels should be analyzed within 2 or more weeks and dosage adjusted accordingly.

1.4. Mechanism of Action

Liptruzet contains ezetimibe and atorvastatin, two lipid-lowering compounds with complementary mechanisms of action. Ezetimibe reduces blood cholesterol by inhibiting the absorption of cholesterol by the small intestine. Atorvastatin lowers plasma cholesterol and lipoprotein levels by inhibiting HMG-CoA reductase and cholesterol synthesis in the liver and by increasing the number of hepatic LDL receptors on the cell-surface to enhance uptake and catabolism of LDL; atorvastatin also reduces LDL production and the number of LDL particles.

1.5. Side Effects

Adverse effects associated with the use of Liptruzet includes: increased ALT, increased AST, musculoskeletal pain.

2. NYMALIZE (NIMODIPINE)

2.1. Company

Arbor Pharmaceuticals; Approved by May 2013

2.2. Treatment Area

Reduction of incidence and severity of ischemic deficits following subarachnoid hemorrhage

2.3. General Information

Nymalize (nimodipine) is an oral solution formulation of nimodipine, a dihydropyridine calcium channel blocker. The precise mechanism of action of nimodipine in reducing the incidence and severity of ischemic deficits in adult patients with SAH from ruptured intracranial berry aneurysms is unknown. It is specifically indicated for the improvement of neurological outcome by reducing the incidence and severity of ischemic deficits in adult patients with subarachnoid hemorrhage (SAH) from ruptured intracranial berry aneurysms regardless of their post-ictus neurological condition. It is supplied as a solution for oral administration. It should only be administered via the oral, nasogastric tube, or gastric tube route. The recommended oral dosage is 20 mL (60 mg) every 4 hours for 21 consecutive days.

2.4. Mechanism of Action

Nimodipine is a dihydropyridine calcium channel blocker. The contractile processes of smooth muscle cells are dependent upon calcium ions, which enter these cells during depolarization as slow ionic transmembrane currents. Nimodipine inhibits calcium ion transfer into these cells and thus inhibits contractions of vascular smooth muscle. The precise mechanism of action of nimodipine in reducing the incidence and severity of ischemic deficits in adult patients with SAH from ruptured intracranial berry aneurysms is unknown.

2.5. Side Effects

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Adverse effects associated with the use of Nymalize includes: hypotension, headache, nausea, bradycardia

3. MEKINIST (TRAMETINIB)

3.1. Company
GlaxoSmithKline; Approved by May 2013

3.2. Treatment Area
Unresectable or metastatic melanoma with BRAF V600E or V600K mutations

3.3. General Information
Mekinist (trametinib) is an orally bioavailable inhibitor of mitogen-activated protein kinase kinase (MEK) with potential antineoplastic activity. It specifically binds to and inhibits MEK 1 and 2, resulting in an inhibition of growth factor-mediated cell signaling and cellular proliferation in various cancers. MEK 1 and 2, dual specificity threonine/tyrosine kinases often up regulated in various cancer cell types, play a key role in the activation of the RAS/RAF/MEK/ERK signaling pathway that regulates cell growth. It is specifically indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. It is not indicated for patients who have received prior BRAF-inhibitor therapy. It is supplied as a tablet for oral administration. The recommended dose is 2 mg orally once daily until disease progression or unacceptable toxicity. Take at least 1 hour before or 2 hours after a meal. Do not take a missed dose within 12 hours of the next dose.

3.4. Mechanism of Action
Mekinist (trametinib) is a reversible inhibitor of mitogen-activated extracellular signal regulated kinase 1 (MEK1) and MEK2 activation and of MEK1 and MEK2 kinase activity. MEK proteins are upstream regulators of the extracellular signal-related kinase (ERK) pathway, which promotes cellular proliferation. BRAF V600E mutations result in constitutive activation of the BRAF pathway which includes MEK1 and MEK2. It inhibits BRAF V600 mutation-positive melanoma cell growth in vitro and in vivo.

3.5. Side Effects
Adverse events associated with the use of Mekinist includes: rash, diarrhea, lymphedema

4. TAFINLAR (DABRAFENIB)

4.1. Company
GlaxoSmithKline; Approved by May 2013

4.2. Treatment Area
Unresectable or metastatic melanoma with BRAF V600E mutation

4.3. General Information
Tafinlar (dabrafenib) is specifically indicated for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E mutation as detected by an FDA-approved test. It is not indicated for treatment of patients with wild-type BRAF melanoma. It is supplied as a capsule for oral administration. The recommended dose is 150 mg orally taken twice daily, approximately 12 hours apart, until disease progression or unacceptable toxicity occurs. Take either at least 1 hour before or at least 2 hours after a meal. A missed dose can be taken up to 6 hours prior to the next dose.

4.4. Mechanism of Action
Tafinlar (dabrafenib) is an inhibitor of some mutated forms of BRAF kinases, as well as wild-type BRAF and CRAF kinases. Some mutations in the BRAF gene, including those that result in BRAF V600E, can result in constitutively activated BRAF kinases that may stimulate tumor cell growth.

4.5. Side Effects
Adverse events associated with the use of Tafinlar includes: hyperkeratosis, headache, pyrexia, arthralgia, papilloma, alopecia, palmar-plantar erythrodysesthesia syndrome.

5. BREO ELLIPTA (FLUTICASONE FUROATE AND VILANTEROL INHALATION POWDER)

5.1. Company
GlaxoSmithKline; Approved by May 2013

5.2. Treatment Area
Chronic obstructive pulmonary disease

5.3. General Information
BreoEllipta is specifically indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema. It is also indicated to reduce exacerbations of COPD in patients with a history of exacerbations. It is supplied as a powder for inhalation. The recommended dose is 100 mcg/25 mcg administered as 1 inhalation once daily by the orally inhaled route only. After inhalation, the patient should rinse his/her mouth with water without swallowing to help reduce the risk of oropharyngeal candidiasis. It should be taken at the same time every day. Do not use more than 1 time every 24 hours.

5.4. Mechanism of Action
Breo Ellipta is a combination of fluticasone furoate, an inhaled corticosteroid (ICS), and vilanterol, a long-acting beta2-adrenergic agonist (LABA).

5.5. Side Effects
Adverse events associated with the use of Breo Ellipta includes: nasopharyngitis, upper respiratory tract infection, headache, oral candidiasis, Actemra ((ocilizumab).

6. ACTEMRA (TOCILIZUMAB)

6.1. Company
Genentech; Approved by May 2013

6.2. Treatment Area
Polyarticular Juvenile Idiopathic Arthritis

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6.3. General Information
Actemra (tocilizumab) is a humanized anti IL-6 receptor monoclonal antibody. It binds specifically to IL-6 receptors. IL-6 is a pro-inflammatory cytokine produced by a variety of cell types, including T- and B-cells, lymphocytes, monocytes and fibroblasts. It is specifically approved for patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis. It is supplied as a solution for intravenous administration. Actemra may be used alone or in combination with methotrexate. The recommended dose of for PJIA patients is once every 4 weeks as a 60-minute single intravenous drip infusion: patients less than 30 kg weight: 10 mg per kg; patients at or above 30 kg weight: 8 mg per kg.

6.4. Mechanism of Action
Actemra is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody of the immunoglobulin IgG1 (gamma 1, kappa) subclass. Tocilizumab binds specifically to both soluble and membrane-bound IL-6 receptors and has been shown to inhibit IL-6-mediated signaling through these receptors. IL-6 is a pleiotropic pro-inflammatory cytokine produced by a variety of cell types including T- and B-cells, lymphocytes, monocytes and fibroblasts. IL-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis.

6.5. Side Effects
Adverse effects associated with the use of Actemra includes: upper respiratory tract infections, nasopharyngitis, headache, hypertension, increased ALT

7. ILARIS (CANAKINUMAB)

7.1. Company
Novartis; Approved by May 2013

7.2. Treatment Area
Systemic Juvenile Idiopathic Arthritis

7.3. General Information
Ilaris is specifically indicated for the treatment of active Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older. It is supplied as a lyophilized powder for solution for subcutaneous injection. The recommended dose for SJIA patients with a body weight greater than or equal to 7.5kg is 4mg/kg (with a maximum of 300mg) administered every four weeks.

7.4. Mechanism of Action
Ilaris (canakinumab) is a human monoclonal anti-human IL-1ß antibody. Canakinumab binds to human IL1ß and neutralizesits activity by blocking its interaction with IL-1 receptors, but it does not bind IL-1a or IL-1 receptor antagonist (IL-1ra).

7.5. Side Effects
Adverse effects associated with the use of Ilaris for SJIA includes: infections (nasopharyngitis and upper respiratory tract infections), abdominal pain, injection site reactions.

8. SIMPONI (GOLIMUMAB)

8.1. Company
Janssen Biotech; Aproved by May 2013

8.2. Treatment Area
Ulcerative colitis

8.3. General Information
Simponi (golimumab) blocks tumor necrosis factor (TNF), which plays an important role in causing abnormal inflammatory and immune responses. It is specifically indicated for moderately to severely active ulcerative colitis in patients who have demonstrated corticosteroid dependence or who have had an inadequate response to or failed to tolerate oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine. The recommended dose is a 200 mg subcutaneous injection at Week 0, followed by 100 mg at Week 2 and then maintenance therapy with 100 mg every 4 weeks.

8.4. Mechanism of Action
Simponi (golimumab) is a human IgG1k monoclonal antibody specific for human tumor necrosis factor alpha (TNFa). It was created using genetically engineered mice immunized with human TNF, resulting in an antibody with human-derived antibody variable and constant regions. Simponi is produced by a recombinant cell line cultured by continuous perfusion and is purified by a series of steps that includes measures to inactivate and remove viruses.

8.5. Side Effects
Adverse events associated with the use of Simponi includes: upper respiratory tract infection, nasopharyngitis, injection site reactions.

9. KCENTRA (PROTHROMBIN COMPLEX CONCENTRATE)

9.1. Company
CSL Behring; Approved by May 2013

9.2. Treatment Area
Reversal of vitamin K antagonist therapy-induced coagulation factor deficiency

9.3. General Information
Kcentra is specifically indicated for for the urgent reversal of acquired coagulation factor deficiency induced by Vitamin K antagonist (VKA, e.g., warfarin) therapy in adult patients with acute major bleeding. It is supplied as a solution for intravenous administration. Kcentra dosing is based on the patient's current pre-dose International Normalized Ratio (INR) value, and body weight. Administer Vitamin K concurrently to patients receiving Kcentra.

9.4. Mechanism of Action
Kcentra contains the Vitamin K-dependent coagulation Factors II (FII), VII (FVII), IX (FIX), and X (FX), together known as the Prothrombin Complex, and the antithrombotic Protein C and Protein S.

9.5. Side Effects
Adverse effects associated with the use of Kcentra includes: headache, nausea/vomiting, arthralgia, hypotension.

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10. PROCYSBI (CYSTEAMINE BITARTRATE)

10.1. Company
Raptor Pharmaceuticals; Approved by May 2013

10.2. Treatment Area
Nephropathic cystinosis

10.3. General Information
Procysbi is specifically indicated for the management of nephropathic cystinosis in adults and children ages 6 years and older. It is supplied as a delayed-release capsule and can be administered either orally or via a feeding tube. It should be taken at least 2 hours after and at least 30 min before eating. The dose should be raised gradually over 4 to 6 weeks to help reduce the risk of side-effects. WBC cystine level and/or cysteamine concentration measurements, taken ½ hour after dose administration, are recommended for new patients after the maintenance dose is achieved. Maintenance Dose: The recommended maintenance dose is 1.3 gram/m2/day, in two divided doses given every 12 hours. The dose can be increased up to 1.95 grams/m2/day if the white blood cell cystine level remains higher than the target WBC cystine level and/or the target cysteamine concentration have not been achieved.

10.4. Mechanism of Action
Procysbi (cysteamine bitartrate)) delayed-release capsules is a cystine depleting agent which lowers the cystine content of cells in patients with nephropathic cystinosis, an inherited defect of lysosomal transport. Cysteamine is an aminothiol that participates within lysosomes in a thiol-disulfide interchange reaction converting cystine into cysteine and cysteinecysteamine mixed disulfide, both of which can exit the lysosome in patients with cystinosis.

10.5. Side Effects
Adverse effects associated with the use of Procysbi includes: vomiting, abdominal pain/discomfort, headaches, nausea, diarrhea, anorexia/decreased appetite, breath odor, fatigue, dizziness, skin odor, rash.

11. XOFIGO (RADIUM RA 223 DICHLORIDE)

11.1. Company
Bayer Healthcare Pharmaceuticals; Approved by May 2013

11.2. Treatment Area
Prostate cancer with bone metastases

11.3. General Information
Xofigo is specifically indicated for the treatment of patients with castration-resistant prostate cancer, symptomatic bone metastases and no known visceral metastatic disease. It is supplied as a solution for intravenous administration. The recommended dose is s 50 kBq (1.35 microcurie) per kg body weight, given at 4 week intervals for 6 injections.

11.4. Mechanism of Action
Xofigo (radium Ra 223 dichloride), an alpha particle-emitting pharmaceutical, is a radiotherapeutic drug. Radium Ra 223 dichloride, which mimics calcium and forms complexes with the bone mineral hydroxyapatite at areas of increased bone turnover, such as bone metastases. The high linear energy transfer of alpha emitters leads to a high frequency of double-strand DNA breaks in adjacent cells, resulting in an anti-tumor effect on bone metastases. The alpha particle range from radium-223 dichloride is less than 100 micrometers which limits damage to the surrounding normal tissue.

11.5. Side Effects
Adverse events associated with the use of Xofigo includes: nausea, diarrhea, vomiting, peripheral edema.

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