Specialty Products Recently Approved

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<th>Drug Name</th>
<th>Manufacturer</th>
<th>FDA Approval Date</th>
<th>Therapeutic Use</th>
<th>Potential Impact</th>
<th>UM Program Available*</th>
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<td>Takeda</td>
<td>May 19, 2014</td>
<td>Crohn’s disease</td>
<td>Low</td>
<td>PA</td>
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<td>Eloctate (Factor VIII Fc fusion protein)</td>
<td>Biogen</td>
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<td>Hemophilia A</td>
<td>Low</td>
<td>PA</td>
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*UM: Utilization Management
QL: Quantity limit designed to encourage appropriate drug use and contain drug cost
PA: Prior authorization designed to ensure appropriate use of potentially expensive, limited use or inappropriately utilized drugs
PG: Pharmacogenomics designed to ensure appropriate drug use of potentially expensive, limited use or inappropriately utilized drugs through genetic testing
ST: Step therapy designed to promote use of safe and cost-effective drugs prior to utilizing more costly drug therapy

**Entyvio™ (vedolizumab) – Takeda**
On May 19, 2014, the U.S. Food and Drug Administration (FDA) approved Entyvio, a humanized monoclonal antibody for the treatment of moderate to severe Crohn’s disease (CD) and ulcerative colitis (UC) in patients who have tried and failed a tumor necrosis factor blocker, immunomodulator, or corticosteroid. Entyvio is not first-line therapy and falls later in the treatment algorithm. Although there have been no cases of patients developing a rare, but often fatal, brain infection known as progressive multifocal leukoencephalopathy (PML) with Entyvio, PML and death have occurred in patients treated with another similar agent, Tysabri® (natalizumab). Current FDA approved therapies for CD and UC include Cimzia® (certolizumab), Humira® (adalimumab), Simponi® (golimumab), Remicade® (infliximab) and Tysabri.

**Eloctate™ (Factor VIII Fc fusion protein) – Biogen Idec and Swedish Orphan Biovitrum**
Eloctate, a long lasting clotting factor, was approved for use in adults and children to treat hemophilia A (Factor VIII deficiency). Hemophilia A is an inherited blood-clotting disorder that can lead to prolonged or spontaneous bleeding with life-threatening consequences. Compared to other available therapies, such as Advate®, Helixate® FS, Kogenate® FS, Recombinate®, ReFacto® and Xyntha®, Eloctate is dosed less frequently, typically once a week via injection. A clinical trial found that Eloctate was effective in treating bleeding episodes when compared to conventional on-demand therapy, and there were no safety concerns identified with treatment.

Specialty Products in the Pipeline: 2014

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**Plegridy™ (peginterferon beta-1a) – Biogen**

Plegridy is an investigational drug product in the multiple sclerosis (MS) pipeline. Plegridy is a new formulation of the existing drug product Avonex®. If approved, Plegridy will be dosed once every two or four weeks via subcutaneous injection. The FDA is anticipated to make a decision on August 21, 2014. Earlier this year, Teva Pharmaceuticals received FDA approval for a long-acting version of Copaxone® which is administered three times a week. Approval of long-acting formulations will likely transform the way individuals suffering with MS approach their treatment, as well as the rates of adoption by both physicians and patients, due to reduced dosing.

**Brand Name to be Determined (idelalisib) – Gilead**

Idelalisib is an investigational oral inhibitor of phosphoinositide 3-kinase (PI3K) delta. PI3K-delta is critical for the activation, proliferation and survival of cancer cells. Idelalisib is pending approval for the treatment of indolent non-Hodgkin’s lymphoma (NHL) and as second-line treatment of chronic lymphocytic leukemia (CLL). Approval for these indications could come as early as August and September 2014, respectively. Current therapies for NHL and CLL include Rituxan® (rituximab), Treanda® (bendamustine) and Arzerra® (ofatumumab). In October 2013, an independent Data Monitoring Committee recommended the discontinuation of a Phase III study evaluating idelalisib in previously treated CLL patients who were not fit for chemotherapy. The discontinuation was based on analysis showing high efficacy for progression-free survival in patients receiving idelalisib plus rituximab, compared to those receiving rituximab alone.  

**Lemtrada® (alemtuzumab) – Genzyme**

In December 2013, the FDA provided a complete response letter and denied approval for Lemtrada (alemtuzumab), an anti-CD52 monoclonal antibody for the treatment of MS. Alemtuzumab, also available under the brand name Campath, is currently approved for the treatment of CLL, but Genzyme has limited distribution so it is not used for treatment of MS prior to FDA approval. The FDA stated Genzyme had not provided sufficient evidence from adequate and well-controlled studies to demonstrate that the benefits of treatment outweigh Campath’s serious adverse effects. On May 30, 2014, the FDA accepted Genzyme’s resubmission of Letrada for approval. The FDA is anticipated to make a decision in the fourth quarter of 2014.

**Brand Name to be Determined (ABT-450/ritonavir/ombitasvir/dasabuvir) – AbbVie and Enanta**

On June 13, 2014, the FDA granted priority review for this fixed-dose combination product for treatment-naïve and treatment-experienced adults with genotype 1 hepatitis C. Priority review designation means the FDA will likely decide within six months whether to approve the regimen. If approved, it’s likely this regimen will compete with the once daily investigational, oral combination of sofosbuvir (Sovaldi®) and ledipasvir. Recently, full data on the Phase III SAPPHIRE I
and II trials was presented, which evaluated hepatitis C treatment-naïve (N=631) and treatment-experienced (N=394) genotype 1 patients. The sustained virology response (SVR), or attainment of undetectable virus levels in the blood, was reached six months after therapy had ended, with 12 weeks of treatment was 96 percent for both studies. The PEARL-III and PEARL-IV showed that patients with hepatitis C virus (HCV) genotype-1a had a 97% SVR after 12 weeks of treatment with the four drug combination. For patients with HCV genotype-1b, the SVR was 99%, with or without ribavirin. If approved, patients will need to undergo hepatitis C genotyping prior to starting treatment with this medication, as this product will be included in WellDyneRx’s Personalized Medicine program.

**Brand Name to be Determined (daclatasvir/asunaprevir) – Bristol-Myers Squibb**
Daclatasvir, a NS5A inhibitor, is currently being studied in more than 5,000 patients as part of a combination regimen with peginterferon alfa (Pegasys®, Peg-Intron®) and ribavirin, as well as asunaprevir and Sovaldi. The NS5A protein plays a key role in the replication and growth of the hepatitis C virus, and drug study data has demonstrated the addition of daclatasvir to peginterferon alfa and ribavirin, compared with peginterferon alfa and ribavirin alone, increased SVR in patient’s naïve to therapy at treatment weeks 12 and 24. Other studies have demonstrated that a peginterferon-free combination of daclatasvir and asunaprevir, an investigational protease inhibitor similar to Incivek® and Victrelis™, is effective in eliminating the virus in patients who failed to respond to previous treatment. Treatment with daclatasvir was generally safe and well-tolerated, and the FDA is expected to decide on approval in the fourth quarter of 2014. If approved, patients will need to undergo hepatitis C genotyping prior to starting treatment with daclatasvir, as this product will be included in WellDyneRx’s Personalized Medicine program.

**Brand Name to be Determined (ledipasvir/sofosbuvir) – Gilead**
Gilead is developing a fixed-dose combination product featuring ledipasvir and sofosbuvir in an oral tablet formulation for the treatment of hepatitis C. In February 2014, Gilead submitted a new drug application to the FDA for the treatment of genotype-1 chronic hepatitis C, and approval is expected by October 2014. Results from the ELECTRON2, an ongoing, open-label Phase II clinical trial, evaluating a once-daily combination of sofosbuvir 400mg and ledipasvir 90mg, with and without ribavirin, were announced in April 2014. In this study, 100 percent of treatment-naïve genotype-3 patients receiving 12 weeks of ledipasvir and sofosbuvir, plus ribavirin, achieved SVR after completing 12 weeks of therapy. Among patients with genotype-1 who had failed prior treatment with sofosbuvir plus ribavirin, 100 percent achieved SVR following 12 weeks of treatment with the combination tablet and ribavirin. Ledipasvir and sofosbuvir, with and without ribavirin was well-tolerated, including patients with more advanced liver disease. In May 2014, results from the Phase III clinical trial, ION-1, were published in the New England Journal of Medicine and demonstrated that once-daily ledipasvir-sofosbuvir, with or without ribavirin, for 12 or 24 weeks achieved SVR rates of 98-99% in previously untreated patients with HCV genotype-1 infection.

**Brand Name to be Determined (olaparib) – AstraZeneca**
Olaparib is an investigational oral poly (ADP ribose) polymerase (PARP) inhibitor for use in patients who have ovarian cancer, have a breast cancer mutation, and whose cancer has relapsed following a complete or partial response to standard therapy with platinum-based chemotherapy, such as cisplatin or carboplatin with paclitaxel. Based on a Phase II clinical trial, olaparib 400mg twice daily was found to be superior to placebo for progression-free survival in patients previously received treatment with platinum-based chemotherapy. Currently, Hexalen® is the only FDA approved oral medication for the palliative treatment of patients with persistent or recurrent ovarian cancer following treatment with platinum-based chemotherapy. Olaparib was granted priority review by the FDA and approval is expected by October 3, 2014.

**Brand Name to be Determined (secukinumab) – Novartis**
In October 2013, Novartis announced results from the head-to-head FIXTURE trial, which showed secukinumab, and IL-17A inhibitor as being significantly superior to Enbrel® (etanercept) in moderate to severe plaque psoriasis. The FEATURE and JUNCTURE psoriasis studies demonstrated rapid skin clearance as well as positive patient outcomes with self-administration. Additional research is being conducted to study the use of secukinumab in ankylosing spondylitis, psoriatic arthritis and rheumatoid arthritis, with the possibility of an expanded therapeutic role once research is completed. Expected approval by the FDA is anticipated in October 2014.

**TASQ® (tasquinimod) – Active Biotech**
Tasquinimod is an investigational oral drug being studied for the treatment of prostate cancer. In a Phase II clinical trial, tasquinimod was shown to increase progression-free survival by 4.3 months compared to placebo. Based on these results, a larger Phase III trial is underway in 1,200 men with symptomatic metastatic castration-resistant prostate cancer (CRPC). According to the National Comprehensive Cancer Network (NCCN) guidelines, four therapeutic agents have
demonstrated prolonged overall survival in metastatic CRPC: sipuleucel-T (Provenge®), docetaxel, abiraterone (Zytiga®), and cabazitaxel (Jevtana®).

**Brand Name to be Determined (faldaprevir) – Boehringer Ingelheim**

Faldaprevir manufactured by Boehringer Ingelheim is pending FDA approval for the treatment of genotype 1 hepatitis C in combination with peginterferon alfa and ribavirin. Faldaprevir does not represent a new mechanism of action for treating hepatitis C, but a second generation protease inhibitor, similar to simprevir or Olysio™. Unlike simprevir, data from a Phase III clinical trial suggests faldaprevir is effective in patients with a genetic mutation known as the Q80K variant, which can affect up to 50% of genotype-1a in some patient populations.

**Aeroquin™ (levofloxacin) – Aptalis Pharma**

Aeroquin is an aerosolized delivery system for existing antibiotic levofloxacin (Levaquin®) for patients with cystic fibrosis (CF) experiencing recurrent *Pseudomonas aeruginosa* infections. In a Phase III study, Aeroquin demonstrated non-inferiority when compared to tobramycin inhalation systems (TOBI®) and improved lung function. Patients with moderate to severe CF are currently treated with inhaled antibiotics, such as TOBI or Cayston®, and oral azithromycin for chronic *P. aeruginosa* infections. Aeroquin demonstrated safety and tolerability consistent across studies; the most significant adverse event reported was a metallic taste. An extension of one Phase III trial is ongoing, and FDA approval isn't expected until 2016.

**References:**