### Brand Products Recently Approved

<table>
<thead>
<tr>
<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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</thead>
<tbody>
<tr>
<td>Dalvance (dalbavancin)</td>
<td>Durata</td>
<td>May 23, 2014</td>
<td>Skin Infections</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Natesto (testosterone gel, intranasal)</td>
<td>Trimel</td>
<td>May 28, 2014</td>
<td>Low testosterone</td>
<td>Low</td>
<td>PA</td>
</tr>
<tr>
<td>Vogelxo (testosterone gel)</td>
<td>Upsher-Smith</td>
<td>June 4, 2014</td>
<td>Low testosterone</td>
<td>Low</td>
<td>PA</td>
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<td>Bunavail (buprenorphine/naloxone)</td>
<td>BioDelivery</td>
<td>June 10, 2014</td>
<td>Opioid dependence</td>
<td>Low</td>
<td>QL</td>
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<tr>
<td>Sivextro (tedizolid)</td>
<td>Cubist</td>
<td>June 23, 2014</td>
<td>Bacterial infections</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Afrezza (insulin, human)</td>
<td>MannKind</td>
<td>June 27, 2014</td>
<td>Type 1 and 2 diabetes</td>
<td>Low</td>
<td></td>
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</tbody>
</table>

*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
ST: Step therapy designed to promote use of safe and cost-effective drugs prior to utilizing more costly drug therapy

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**Dalvance™ (dalbavancin) – Durata**

On May 23, 2014, the U.S. Food and Drug Administration (FDA) approved Dalvance, an antibiotic, for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible bacteria. ABSSSI includes cellulitis, erysipelas, wound infection, and major skin abscess. These types of infections typically result in lengthy and expensive hospital stays. Dalvance fights gram-positive bacteria, including methicillin-susceptible *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus* and *Streptococcus pyogenes*. Dalvance is administered intravenously with a two-dose regimen over a period of one week, which will promote better adherence over currently available daily regimens, such as Vanc® (vancomycin) and Zyvox® (linezolid).

**Natesto™ (testosterone gel, intranasal) – Trimel**

The FDA approved Natesto for the treatment of hypogonadism, or low testosterone in males. The product is self-administered via a nasal applicator, reducing the risk of secondary exposure of testosterone to women or children. Testosterone replacement therapies available at this time include Axiron™, Androderm®, Androgel®, Fortesta™, Striant™ and Testim®. Currently, there are no long-term clinical studies directly comparing topical testosterone treatment options.

**Vogelxo™ (testosterone gel) – Upsher-Smith**

On June 4, 2014, the FDA approved Vogelxo for the treatment of hypogonadism, or low testosterone in males. Vogelxo shows no clear advantages over currently available topical therapies such as Axiron™, Androderm®, Androgel®, Fortesta™, Striant™ and Testim®, and there are no clinical trials directly comparing the efficacy and safety of the available products. WellDyneRx offers a testosterone step therapy program that contains costs by driving patients to try equally efficacious products that are less expensive.
**Bunavail™ (buprenorphine/naloxone) – BioDelivery Sciences**

Bunavail (buprenorphine/naloxone) is a buccal film formulation of an existing drug product, Suboxone®, for the treatment of opioid dependence. It utilizes a new drug delivery method of placing the buccal film inside the cheek, which allows for better absorption than the sublingual tablets or films currently available on the market. This administration may help reduce the potential for misuse and diversion, as doses using this delivery system are lower than products currently available on the market, although there is no clinical data to verify this and its place in therapy remains unclear.

BioDelivery anticipates launching Bunavail in the third quarter of 2014.

**Sivextro® (tedizolid) – Cubist**

Tedizolid, an intravenous (IV) and oral antibiotic, received FDA approval on June 23, 2014 for the treatment of acute bacterial skin and skin structure infections (ABSSSI) with gram-positive susceptible bacteria, including methicillin-resistant and methicillin-susceptible *Staphylococcus aureus*. Tedizolid will compete with Zyvox and Vanc, and newly approved Dalvance, which are used in patients with serious and life-threatening skin and skin-structure infections who have not responded to other antibiotic agents. It is anticipated patients will begin tedizolid therapy in the hospital via IV and transition to the oral antibiotic for use at home. Tedizolid, administered once-daily for six days, has been found to be non-inferior and have similar adverse effects when compared to Zyvox administered twice-daily for ten days.

**Afrezza® (insulin, human) – MannKind**

Afrezza received FDA approval for the meal-time management of blood sugar in type 1 and type 2 diabetics. If approved, Afrezza will be the second inhaled insulin combination product to be approved by the FDA. Exubera®, approved by the FDA in 2006, was withdrawn from the market 21 months later by drug manufacturer Pfizer due to respiratory safety concerns and poor sales performance. To date, there are no inhaled insulin products available in the market. In April 2014, members of the Endocrinologic and Metabolic Drugs Advisory Committee voted 13 to 1 in favor of approval of Afrezza for type 1 diabetes, and 14 to 0 for approval for type 2 diabetes. The panel noted concerns about the lack of long-term data on lung function beyond two years, and recommended post-marketing studies and labeling requirements. Market launch date and cost information are not available at this time. WellDyneRx is reviewing drug study data for inclusion of utilization management strategies.

**Other FDA Actions**

**MoxDuo™ (morphine/oxycodone) – QRxPharma and Actavis**

On May 27, 2014, QRxPharma received a complete response letter from the FDA denying approval of MoxDuo, stating there was no clear advantage over existing oxycodone and morphine pain medications. This decision comes after following the advice of its advisory panel, which unanimously voted against approving MoxDuo.

**Brand name to be determined (empagliflozin) – Boehringer Ingelheim and Eli Lilly**

Boehringer Ingelheim announced it will resubmit a New Drug Application (NDA) for empagliflozin, an investigational SGLT-2 inhibitor for the treatment of type 2 diabetes, although an exact date is not yet available. The resubmission follows a successful FDA inspection of Boehringer Ingelheim’s manufacturing plant. The FDA denied approval of empagliflozin in March, 2014, citing deficiencies at the manufacturing plant as the reason.

<table>
<thead>
<tr>
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<th>Estimated Launch Date</th>
<th>Therapeutic Use</th>
<th>Potential Impact</th>
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<tbody>
<tr>
<td><strong>Levadex</strong> (dihydroergotamine)</td>
<td>Allergan and MAP</td>
<td>2014</td>
<td>Migraines</td>
<td>Low</td>
</tr>
<tr>
<td><strong>Striverdi Respimat</strong> (olodaterol)</td>
<td>Boehringer Ingelheim</td>
<td>2014</td>
<td>Chronic obstructive pulmonary disease</td>
<td>Low</td>
</tr>
<tr>
<td><strong>TBD</strong> (suvorexant)</td>
<td>Merck</td>
<td>2014</td>
<td>Insomnia</td>
<td>Low</td>
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</table>
Levadex™ (dihydroergotamine) – Allergan and MAP
Levadex is an orally inhaled formulation of the existing product, dihydroergotamine (D.H.E 45 injection and Migranal® nasal spray), used for the management of migraines. The formulation is intended to offer a fast onset of action, similar to an intravenous infusion, but without the need for an injection. In a clinical trial, Levadex provided pain relief from migraines within 30 minutes. Additionally, approximately 50 percent more patients receiving Levadex reported pain relief at ten minutes and relief for up to 48 hours, when compared to those who received a placebo. Treatment with Levadex was well tolerated with no serious adverse events reported, but clinical studies directly comparing migraine treatment options are lacking. The FDA declined to approve dihydroergotamine twice, due to concerns with the manufacturing process of the inhaler used; however, Allergan has begun addressing the FDA’s manufacturing concerns.

Striverdi® Respimat® (olodaterol) – Boehringer Ingelheim
Olodaterol is an ultra-long-acting beta agonist (LABA) pending approval for maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. In clinical trials, patients taking olodaterol showed pulmonary function improvement in three of four 48-week COPD studies. An FDA Pulmonary-Allergy advisory panel recommended 15 to 1 that olodaterol can safely and effectively be used in COPD patients. However, several panel members recommended Boehringer Ingelheim conduct post-marketing studies to monitor tumor development, if approved. Along with Arcapta®, Striverdi offers an advantage over other available LABAs, such as Foradil® (formoterol) or Serevent® (salmeterol), in that it is only dosed once a day as opposed to twice daily. The FDA will most likely approve olodaterol in 2014.

Brand to be determined (suvorexant) – Merck
In November 2012, Merck submitted a NDA for its investigational drug product suvorexant, designed to treat insomnia. It’s likely that the Drug Enforcement Agency will also review the NDA due to its risk for potential abuse. Drug study data demonstrated treatment with suvorexant improved a patient’s ability to fall and stay asleep, decreased drowsiness the following day, and had no significant withdrawal symptoms. An independent advisory panel voted 13 to 3 in favor of recommending suvorexant in two different drug strengths. However, the panel was split when it came to approving the higher strengths, as they have been associated with increased daytime drowsiness, suicidal thoughts, and difficulty driving, especially in the elderly. On July 1, 2013, the FDA issued a complete response letter citing dosing concerns and determined the 30 and 40mg doses were unsafe requesting Merck conduct additional manufacturing studies for a 10mg strength. Merck is also planning on releasing a 5mg strength. Due to the additional manufacturing studies, Merck hopes the product will be approved and available on the market in the second half of 2014. If approved, suvorexant will compete with zolpidem (Ambien®) and zaleplon (Sonata®), which are sleep medications that are currently available as low-cost generic products.

Contrave® (bupropion, naltrexone) – Orexigen and Takeda
On June 11, 2014, the FDA postponed their final decision on Contrave, an investigational drug being evaluated for weight loss, for at least 3 months. The delay is needed to finalize an agreement between the FDA and Orexigen on tracking cardiovascular side effects post approval. Contrave is a, fixed-dose, investigational combination product of existing medications, Wellbutrin® (bupropion), approved for the treatment of depression, and Revia® (naltrexone), indicated for alcoholism. In 2011, the FDA failed to approve the diet drug due to heart-related safety concerns, and indicated a heart

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<tr>
<td>Contrave (bupropion/naltrexone)</td>
<td>Orexigen and Takeda</td>
<td>3Q 2014</td>
<td>Weight loss</td>
<td>Low</td>
</tr>
<tr>
<td>Orbactiv (oritavancin)</td>
<td>Medicines Company</td>
<td>3Q 2014</td>
<td>Skin infections</td>
<td>Low</td>
</tr>
<tr>
<td>Targiniq ER (oxycodone/naloxone)</td>
<td>Purdue</td>
<td>3Q 2014</td>
<td>Chronic pain</td>
<td>Low</td>
</tr>
<tr>
<td>TBD (dulaglutide)</td>
<td>Eli Lilly</td>
<td>4Q 2014</td>
<td>Type 2 diabetes</td>
<td>Low</td>
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*Estimated launch dates are subject to change due to legal proceedings, exclusivity, timing of FDA approvals, additional patents, etc.
Outcomes study was needed in order to consider approval. Orexigen has submitted provisional cardiovascular data and is working with the FDA to finalize the review.

**Orbactiv (oritavancin) – Medicines Company**

Oritavancin, an investigational intravenous antibiotic, is seeking approval for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible gram-positive bacteria, including methicillin-resistant Staphylococcus aureus, administered as a single dose. Oritavancin is a synthetic analog of Vanco (vancomycin), but it exhibits a long half-life that allows for single dose therapy. In a Phase III clinical trial, oritavancin single-dose was found to be non-inferior to twice-daily vancomycin intravenous infusion for 7 to 10 days, with respect to cure rate and rate of serious adverse side effects. Oritavancin will compete with recently approved Dalvance and Sivextro and is hoped to promote better adherence and potential outpatient treatment over currently available daily regimens, such as Vanco and Zyvox. The FDA is expected to make a decision on oritavancin on August 6, 2014.

**Targiniq™ ER (oxycodone/naloxone extended release) – Purdue**

On November 23, 2013, the FDA accepted a NDA for Targiniq extended release (ER), intended for the management of chronic pain. Targiniq ER combines the potent opioid painkiller, oxycodone, with the opioid antagonist, naloxone. This fixed-dose combination product is suggested to help curb drug abuse and misuse. Clinical abuse studies, along with clinical trial data, showing safety and efficacy was submitted to the FDA for review. The FDA is set to make a decision in September 2014.

**Brand to be determined (dulaglutide) – Eli Lilly**

Dulaglutide is a long-acting, glucagon-like peptide-1 (GLP-1) receptor agonist being studied for once-weekly administration for type 2 diabetes. Data from type 2 diabetes trials showed the administration of dulaglutide was comparable to competitor Victoza® and statistically superior at reducing HbA1c (diagnostic marker of diabetes control) from baseline levels when compared to insulin glargine. In another Phase III clinical trial, dulaglutide was also superior in lowering HbA1c levels and assisting with weight loss when compared to Januvia® (sitagliptin). Treatment with dulaglutide was well tolerated with no serious adverse events reported and will compete with other GLP-1 receptor agonists, including Byetta®, Bydureon®, Victoza®, and Tanzeum®. The FDA is expected to make a decision on October 4, 2014.

**References:**