### 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>
</tr>
</thead>
<tbody>
<tr>
<td>Movantik (naloxegol)</td>
<td>AstraZeneca</td>
<td>September 16, 2014</td>
<td>Opioid-induced constipation</td>
<td>Low</td>
<td>PA, QL</td>
</tr>
<tr>
<td>Akynzeo (netupitant/palonosetron)</td>
<td>Helsinn Healthcare</td>
<td>October 10, 2014</td>
<td>Chemotherapy induced nausea and vomiting</td>
<td>Low</td>
<td>PA, QL</td>
</tr>
<tr>
<td>Xigduo XR (dapagliflozin/metformin)</td>
<td>AstraZeneca</td>
<td>October 29, 2014</td>
<td>Type 2 diabetes</td>
<td>Low</td>
<td>QL</td>
</tr>
<tr>
<td>Hysingla ER (hydrocodone extended-release)</td>
<td>Purdue</td>
<td>November 20, 2014</td>
<td>Pain</td>
<td>Low</td>
<td>QL</td>
</tr>
<tr>
<td>Namzaric (donepezil/ memantine extended-release)</td>
<td>Forest</td>
<td>December 24, 2014</td>
<td>Alzheimer’s disease</td>
<td>Low</td>
<td>QL</td>
</tr>
<tr>
<td>Saxenda (liraglutide)</td>
<td>Novo Nordisk</td>
<td>December 24, 2014</td>
<td>Obesity</td>
<td>Low</td>
<td>PA, QL</td>
</tr>
</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

**Movantik® (naloxegol) – AstraZeneca**
Naloxegol is indicated for the treatment of opioid-induced constipation in adults taking opioid medications for a minimum of four weeks. Naloxegol targets the gastrointestinal tissues without penetrating the central nervous system, preventing potential abuse and fewer side effects. The U.S. Food and Drug Administration (FDA) has determined there is no risk of abuse or dependency with naloxegol; however, the Drug Enforcement Agency (DEA) has classified Naloxegol as a schedule-II controlled substance due to its chemical structure, which is very similar to noroxymorphone, an opioid painkiller. The DEA is reviewing AstraZeneca’s request to reclassify Naloxegol, and a decision is expected prior to quarter 1, 2015, when the medication is expected to become available.

**Akynzeo® (netupitant/palonosetron) – Helsinn Healthcare**
On October 10, 2014, the FDA approved the fixed-dose combination product Akynzeo®, indicated for the prevention of chemotherapy induced nausea and vomiting (CINV). Akynzeo is a fixed-dose combination product containing the oral anti-vomiting products netupitant and palonosetron (Aloxi™). Cancer patients undergoing chemotherapy typically experience two types of nausea and vomiting: acute, which occurs within the first 24 hours, and delayed, which happens within 5 days of chemotherapy treatment. Netupitant is a selective substance P neurokinin 1 blocker which prevents CINV in the acute phase and continues working for up to five days to prevent delayed CINV. Palonosetron, a highly selective 5-HT3 receptor blocker, prevents CINV in the acute phase. Recommended dosing is one capsule taken with or without food one hour prior to starting an emetogenic chemotherapy treatment.
Xigduo XR™ (dapagliflozin/ metformin) – AstraZeneca

Xigduo XR™ is a combination product containing Farxiga® (dapagliflozin) and metformin approved for treatment of type 2 diabetes. Dapagliflozin is a sodium-glucose co-transporter 2 (SGLT2) and works by blocking reabsorption of glucose in the kidneys, leading to increased excretion of glucose in the urine. Metformin is the preferred first-line of treatment for diabetic patients, and works by decreasing glucose production while increasing glucose utilization, further reducing the amount of glucose in the blood. Xigduo XR will compete with Invokamet® (canagliflozin/metformin), as well as other oral, anti-diabetic agents in combination with metformin, such as Janumet® and Kombiglyze ER®. SGLT2 inhibitors are considered third-line treatment options and are reserved for patients unable to achieve lower blood glucose levels despite attempting treatment with two or more oral agents.

Hysingla ER® (hydrocodone extended-release) – Purdue

Hysingla ER® is approved for the treatment of chronic, severe pain requiring continuous, long-term treatment for which alternative treatment options are inadequate. It is formulated in a proprietary, abuse-deterrent tablet that is difficult to crush, break or dissolve. When broken, the tablet forms a thick gel and cannot be easily prepared for injection. Hysingla ER will compete with the extended-release, single-ingredient hydrocodone product, Zohydro® ER. Abuse of Hysingla ER is still possible and is not FDA approved for the treatment of as-needed pain relief. Given its risks, Hysingla ER will be added to WellDyneRx’s Pain Guardian: A Fraud, Waste and Abuse program.

Namzaric™ (donepezil/ memantine extended-release) – Forest

Namzaric™ is a, fixed-dose combination product of existing medications, Aricept® (donepezil) and Namenda XR® (memantine extended-release), used to treat Alzheimer’s disease. Namzaric is dosed once-daily and the capsule’s contents may be sprinkled on food for easy administration. Namzaric will compete with Razadyne ER® (galantamine extended-release), Aricept (donepezil), Exelon® (rivastigmine) and Namenda (memantine). With the exception of Namenda, all other therapies are available as generic agents.

Saxenda® (liraglutide) – Novo Nordisk

Saxenda® is a new formulation of the product, Victoza® (liraglutide), a GLP-1 agonist used for treatment of type 2 diabetes. Clinical trials have shown a larger proportion of non-diabetic patients who were prescribed high-dose liraglutide, which is higher than typical dosing for type 2 diabetes, experienced and maintained at least a 5% decrease in body weight from baseline after 56 weeks. Also, about one-third of patients lost more than 10% of their body weight, compared to about 10% of those on placebo. Saxenda, like Victoza, is injected daily. It’s approved for people with a body mass index (BMI) of 30, who are considered obese, or a BMI of 27 with weight-related risk factors such as diabetes or high blood pressure.

### Brand Products in the Pipeline: 2014

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Manufacturer</th>
<th>Estimated Launch Date</th>
<th>Therapeutic Use</th>
<th>Potential Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procoralan (ivabradine)</td>
<td>Amgen</td>
<td>1Q 2015</td>
<td>Heart disease</td>
<td>Low</td>
</tr>
<tr>
<td>Savaysa (edoxaban)</td>
<td>Daiichi Sankyo</td>
<td>1Q 2015</td>
<td>Prevention of blood clots</td>
<td>Low</td>
</tr>
<tr>
<td>Toujeo (insulin glargine)</td>
<td>Sanofi</td>
<td>1Q 2015</td>
<td>Diabetes</td>
<td>Low</td>
</tr>
<tr>
<td>Semprana (dihydroergotamine)</td>
<td>Allergan and MAP</td>
<td>2Q 2015</td>
<td>Migraines</td>
<td>Low</td>
</tr>
</tbody>
</table>
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<tr>
<td><strong>TBD (eluxadoline)</strong></td>
<td>Actavis</td>
<td>2Q 2015</td>
<td>Irritable bowel syndrome</td>
<td>Low</td>
</tr>
<tr>
<td><strong>TBD (brepixiprazole)</strong></td>
<td>Otsuka</td>
<td>3Q 2015</td>
<td>Antipsychotic</td>
<td>Low</td>
</tr>
<tr>
<td><strong>TBD (sacubitril/valsartan)</strong></td>
<td>Novartis</td>
<td>3Q 2015</td>
<td>Heart failure</td>
<td>High</td>
</tr>
</tbody>
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*Estimated launch dates are subject to change due to legal proceedings, exclusivity, timing of FDA approvals, additional patents, etc.

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**Procorolan** (ivabradine) – Amgen

Ivabradine is an oral agent that lowers the heart rate through specific and selective inhibition of the heart’s pacemaker node. Ivabradine is indicated for the treatment of symptoms of long-term, stable angina and in patients with congestive heart failure. Ivabradine has been available in Europe since 2005 and is prescribed for patients whose heart rate is above 60 beats per minute, are in normal sinus rhythm, and cannot be treated with or whose disease is not controlled with beta-blockers. During the SHIFT clinical trial, ivabradine demonstrated a 25% reduction in the risk of death and hospitalization due to heart failure when compared to placebo and standard-of-care treatments. A decision by the FDA is expected by February 27, 2015.

**Savaysa** (edoxaban) – Daiichi Sankyo

Edoxaban™ is an oral, direct factor Xa inhibitor being studied for the prevention and treatment of leg blood clots and atrial fibrillation. Compared to warfarin, which is considered the standard of care, the direct factor Xa inhibitors are administered as a fixed dose, do not require continuous monitoring, and do not have dietary interactions. To date, there are no head-to-head clinical trials comparing edoxaban to other factor Xa inhibitors. In October, 2014, an FDA Advisory Panel voted 9 to 1 in favor of approval of edoxaban for treatment in patients with atrial fibrillation. The FDA is scheduled to meet January 8, 2015, for its final decision regarding approval.

**Toujeo** (insulin glargine) – Sanofi

Toujeo® is a new formulation of an existing insulin product, Lantus® (insulin glargine). Toujeo offers longer duration of action when compared to Lantus, up to 40 hours versus 22 hours. Additionally, clinical trials have demonstrated that Toujeo is better at preventing night-time sugar lows and is comparable to Lantus at lowering blood sugar, whether added to a meal-time insulin regimen or oral anti-diabetic drugs. If approved, Toujeo will compete with Lantus and Levemir® (insulin detemir), and the FDA is expected to make a decision in quarter one, 2015.

**Semprana** (dihydroergotamine) – Allergan and MAP

Semprana™ is an orally inhaled formulation of an existing product, dihydroergotamine used for the management of migraines. The inhaled formulation offers a faster onset of action, similar to an intravenous infusion, but without the need for injections. In a clinical trial, Semprana provided pain relief from migraines within 30 minutes. Treatment was well tolerated with no reported serious adverse events, however, there are no clinical studies directly comparing migraine treatment options. On June 30, 2014, Allergan received a third complete response letter from the FDA, declining approval of their investigational migraine drug, previously known as Levadex, citing concerns with the inhaler’s manufacturing process. Allergan is addressing the FDA’s manufacturing concerns and anticipates an action date in quarter two, 2015.

**Brand Name to be Determined (eluxadoline) – Actavis**

Eluxadoline is an investigational, first-in-class medication indicated for the treatment of diarrhea-predominant irritable bowel syndrome. Eluxadoline works by utilizing two opioid receptor types, mu-opioid receptor agonist and delta opioid receptor antagonists, which play a key role in the gastrointestinal tract. The mu-opioid receptor agonist helps with diarrhea, while the delta opioid receptor antagonist assists with abdominal pain Eluxadoline will likely compete with Lotronex® (alosetron), as well as generically available antispasmodic agents, such as loperamide, diphenoxylate/atropine, and dicyclomine. A decision by the FDA is expected in June, 2015.
Brand Name to be Determined (brexpiprazole) – Otsuka

Brexiprazole is an investigational, second-generation antipsychotic agent being studied for the treatment of schizophrenia and as an adjunctive treatment for major depressive disorder. It’s structure is similar to Abilify® (aripiprazole), a widely-used antipsychotic agent, and will compete with second-generation antipsychotics, such as Risperdal® (risperidone), Zyprexa® (olanzapine) and Seroquel® (quetiapine). No clinical trials have been conducted to demonstrate superiority over available treatment options, many of which are available generically. Approval could come as early as the quarter 3, 2015, but use will likely be limited until additional clinical data is obtained.

Brand Name to be Determined (sacubitril/valsartan) – Novartis

Sacubitril/valsartan is an investigational fixed-dose combination product of two medications, sacubitril and valsartan (Diovan®), being studied for use in patients with heart failure and hypertension. Heart failure will be the lead indication in development. Valsartan is an angiotensin receptor blocker, while sacubitril is a first-in-class neprilysin inhibitor, which lowers blood pressure and works on the brain’s hormones. In a recent clinical trial in heart failure patients, sacubitril/valsartan was superior to enalapril in preventing heart-related complications. Most importantly, the difference in favor of sacubitril/valsartan was seen early. This oral therapy product is targeted as a potential blockbuster medication. Novartis intends on submitting a new drug application in 2014, with possible approval in quarter 3, 2015.

References:


