Specialty Pipeline: Blockbusters on the Horizon

New agents anticipated for liver disease, HIV, cancer and more
We consistently hear from our PBM clients that specialty drugs are one of their primary—if not the top—concerns. These drugs are used to treat complex, chronic conditions, and often require special handling and administration. Not surprisingly, management of these costly therapies is challenging. Because you have entrusted us with the responsibility to help you manage your spend, we have been very strategic in our approach to these high-cost prescription medications.

We work continuously to help you respond to potential blockbusters such as the PCSK9 inhibitors. CVS Health, as an enterprise, has also been strategic about expanding our assets to help you better address specialty spend—embedding care management nurses with our CareTeams, automating medical claims processing to better manage specialty drug costs under the medical benefit, and providing alternative sites of care to manage costs for infused therapies.

In future Executive Briefings we will provide additional updates on the specialty pipeline and on our management approach. If you would like to review how our specialty management capabilities could further address your specific concerns, I urge you to contact your account team to set up an in-depth discussion.

Sincerely,

Alan Lotvin, MD
Executive Vice President, CVS Specialty
CVS Caremark® analysts project that specialty drugs will account for 50 percent of all prescription spending—under both the pharmacy and medical benefit—by 2018. Spend on specialty pharmaceuticals has been growing at double-digit rates for several years and has been a significant contributor to overall trend. This ongoing growth of spending on specialty pharmaceuticals continues to be a challenge for clients.

The robust specialty pipeline is one of the major drivers of this growth. New drugs typically increase utilization, and high prices at launch are common, particularly for innovative products offering new or more effective treatments. Our internal analysis indicates that specialty drugs launched in just the last three years (2013–2015), including the new hepatitis C therapies, accounted for 3.9 percent of 2015 trend.

**Up Next**
According to our analysis, by 2018, the U.S. Food and Drug Administration (FDA) could approve 200 new drugs and 138 new indications. Some of these anticipated launches will be first-in-class therapies. Some will increase category competition. A few have the potential to become blockbusters. All are likely to impact drug spend.
Liver Disease
Leading the group of potential blockbuster drugs—projected annual sales over $1 billion—is obeticholic acid (OCA, brand name Ocaliva™). Ocaliva is an oral treatment expected to be approved this year for an indication of primary biliary cirrhosis (PBC). PBC is a rare, autoimmune disease that destroys the bile ducts in the liver.

The real blockbuster potential for Ocaliva is expected to come later with approval for a second indication for the treatment of nonalcoholic steatohepatitis (NASH). Ocaliva has received a breakthrough designation from the FDA for this second indication, which is a much higher-incidence condition with no currently approved treatment. A breakthrough designation can help speed the review and approval process.

Industry analysts anticipate that the sales for the drug will start slow, but accelerate rapidly if Ocaliva receives the NASH indication, reaching more than $2 billion by 2020. Additional agents for NASH are in the development pipeline, but near-term approval is not expected.

Oncology
More than half the specialty products in clinical development target various kinds of cancer. What’s more, nearly half of those products in the pipeline are considered to be first-in-class oncology therapies. If approved, these treatments are likely to be launched without competition. However, some of the drugs in the pipeline could enhance management opportunities for payors by introducing competition into some cancer treatment classes.

Significant among them is imatinib, the first generic for the reference brand Gleevec®, which launched in February 2016. Like Gleevec, imatinib is indicated for the treatment of chronic myeloid leukemia (CML).

Since only one drug manufacturer currently has market approval to sell generic imatinib in the United States, this generic is priced only slightly lower than Gleevec. Market exclusivity for this newly approved generic expires on August 1, 2016, at which point one or more additional manufacturers may gain FDA clearance, thereby increasing competition and potentially lowering prices. Additional generic treatment options would be expected to help lower the price further in the future.

HIV
Anti-retroviral therapy for HIV is an active area of development for drug manufacturers. The current therapies, which combine several agents in a single pill, are generally effective and well-tolerated. For many of these combination products, the individual agents are losing exclusivity. That raises the potential for generic products with additive adherence support.

Manufacturers continue to develop new formulations, some of which could be potential blockbusters. Three new drugs to treat HIV could be approved this year. The anticipated new products are combination, fixed-dose products that that may provide enhanced safety and lower toxicity for patients.
Other Notable Potential Launches
The 2016 specialty pipeline also contains potential new agents for multiple sclerosis, hepatitis C, psoriasis, and rheumatoid arthritis. The first specialty agent for Parkinson’s Disease psychosis could be approved in the near future, and a new treatment for atopic dermatitis could be approved in early 2017, marking the first use of a specialty agent for this condition. The introduction of specialty agents into new therapeutic classes requires careful management, particularly when the targeted condition is currently treated with relatively low-cost, non-specialty agents and generics.

Biosimilars
The approval of Inflectra™ in early April 2016 marks the FDA’s second approval of a biosimilar. Inflectra, a biosimilar of infliximab (brand name, Remicade®), is approved to treat all but one of the reference drugs’ indications. These include Crohn’s disease, ulcerative colitis, and some forms of rheumatoid arthritis and psoriasis.

FDA approval means that Inflectra and Zarxio®—biosimilar for Neupogen®—are considered safe and effective. The agents have not received a designation of “interchangeability,” which would make it easier to substitute the biosimilar for the reference brand. In 2016, the FDA could also approve biosimilars for Epogen® and Neulasta®—two drugs that respectively boost red and white blood cell production in patients undergoing treatment for cancer.

It’s important to note that the biosimilar market is complicated. As with traditional generic market entrants, patent litigation and legal requirements can delay the launch of approved products significantly. Zarxio, which was approved in March 2015, did not come to market until six months after it won FDA approval. Watch for more information on biosimilars in an upcoming issue of the Insights Executive Briefing.

2016 Significant Specialty Drug Approvals and Pipeline Highlights

<table>
<thead>
<tr>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>June</th>
<th>July</th>
<th>Aug</th>
<th>Sept</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
<th>2nd Half</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCV</td>
<td>Zepatier™*</td>
<td>Asthma</td>
<td>Cinqair™**</td>
<td>HIV</td>
<td>Odefsey®**</td>
<td>Autoimmune</td>
<td>Taltz®**</td>
<td>Neurology</td>
<td>Austed®*</td>
<td>Autoimmune</td>
<td>brodalumab</td>
<td>Rheumatoid</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>sarilumab</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DMD (Duchenne muscular dystrophy), HIV (human immunodeficiency virus), HCV (hepatitis C virus), MS (multiple sclerosis), PBC (primary biliary cirrhosis)

*Approved  †Specialty generic drug

Current as of 04/15/16. Pipeline Services, April 2016. Date provided is either FDA-established PDUFA date or best internal estimates from Pipeline Services.

Dates included in this slide are reflective of likely FDA approval date (otherwise known as PDUFA date). Actual approval date may occur before or after the date shown on this slide.

Some drugs may not gain FDA approval at all. Dates do not reflect a projection for actual market availability. Drug launch may in some cases occur several months after FDA approval.
By the time of its launch, each new product has typically been under our surveillance for three to four years. The surveillance involves a thorough review of available clinical research. We also seek input from external thought leaders, including the Centers for Medicare & Medicaid Services, to help ensure we have a comprehensive perspective.

This in-depth analysis is used to help model impact by client segment. Proactive client briefings and alerts about upcoming specialty drug approvals and launches help to keep you, as the client, informed as new information becomes available.

Ongoing collaboration with our clients enhances transparency and helps us formulate strategic plan design options and better solutions.

Key to our approach is a new-to-market review. We assess clinical appropriateness and cost effectiveness for each new agent prior to making a formulary decision.

We take a variety of factors into consideration including price, competition and whether the drug has received a breakthrough designation from the FDA. Our client-specific modeling is based on market insights and an analysis of your member population and lines of business.

This comprehensive view helps us develop proactive recommendations to help you mitigate trend impact in your plan.

We continue to monitor clinical information about new launches in order to enable your account teams to share insights and provide ongoing consultation based on internal and external best practices.

CVS Health will be piloting a Specialty Pipeline Protection Program early next year. The program could offer clients who have put appropriate specialty management programs in place additional protection from the volatility often caused by costly new specialty drugs and will enhance their ability to better budget for them appropriately.
Formulary Strategy
Evaluation of safety and efficacy forms the foundation of formulary product selection. Within a category of clinically appropriate options, we select the product with the lowest-net cost as the preferred agent in a category. We help our clients integrate clinically appropriate utilization management (UM) criteria and rigorous approval requirements based on therapy options for the entire category.

For example, with the launch of the PCSK9 inhibitors, we recommended that clients’ UM strategy strongly favor the use of cost-effective statins and incorporate a requirement for objective, clinically based evidence of the need for these newer, high-cost agents to control cholesterol.

Medical Benefit Management
Fifty percent of specialty drug spend is administered under the medical benefit, where utilization can be less visible and more difficult to manage. CVS Specialty has unique solutions that can help clients manage this aspect of spend with greater precision.

Our suite of medical benefit management tools enables us to deliver a condition-level management approach to help manage specialty drug spend across benefits, and deliver the lowest-net-cost, most appropriate therapy for an individual patient at a particular stage of treatment. With automated medical claims review, we can help create incremental savings opportunities.

We can also offer alternative, lower-cost sites of care for infusions and the support of specially trained nurses who can help promote earlier hospital discharges and reduce readmissions.

Drug-specific Clinical Strategy
Each specialty drug requires a unique clinical approach. We evaluate how to best support patients who might be prescribed that drug prior to launch in order to have appropriate resources in place. For example, for CML patients prescribed imatinib, we expanded patient-level clinical support with Care Management nurses and our Oncology CareTeam. We also implemented a two-way text message program to help support adherence and safety. Such programs help to ensure appropriate utilization and optimal outcomes from use of the agent.

Each new specialty drug is unique and demands a differentiated approach based on the market landscape as well as the product’s clinical properties and potential
Insights is a series of communications focused on providing context and perspective about key pharmacy and health care topics. Payers continually face new challenges such as volatility in the pharmaceutical market, costly new treatments and regulatory changes. The Insights Executive Briefing is intended to support our clients in understanding and managing the impact of new marketplace developments to help them achieve their goals of lowering costs while improving the health of their plan members.

You can subscribe to the Insights Executive Briefing by emailing insights@cvscaremark.com