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Trends in Specialty Pharmaceuticals

(Source: An article prepared by Aubrey Westgate and published by Managed Healthcare Executive)

Approvals of specialty pharmaceuticals have far outpaced traditional drugs, and that trend will continue. But that's not the only specialty medication trend that healthcare executives should have on their radar. Aimee Tharaldson, PharmD, senior clinical consultant, emerging therapeutics, at Express Scripts, explained, during a recent presentation, how the growth in specialty medications is affecting managed care pharmacy. Here are five noteworthy specialty medication trends Tharaldson identified during her presentation:

1. Specialty approvals will continue to outpace traditional medications. For the past six years the FDA has approved more specialty than traditional medications. Last year, 56 new drugs were approved, 33 of which were specialty medications;

2. Specialty medications will face more competition. Competition in specialty medications is growing (including among generic specialty medications), as more medications are approved, and as more medications impact orphan conditions and cancer. It was also noted that biosimilars could increase competition, once they overcome "litigation hurdles;"

3. Biosimilars are gaining traction. The FDA has approved four biosimilars and many more are in the pipeline. The approved biosimilars are:

- Sandoz's *Zarxio* (filgrastimsndz), approved in March 2015 and launched in September 2015. This is a non-interchangeable biosimilar to Amgen's *Neupogen* (filgrastim). It is approved for neutropenia, and has a wholesale list price 15% less than Neupogen, said Tharaldson.
- *Inflectra* (infliximabdyyb), from Pfizer, approved in April 2016. This is a non-interchangeable biosimilar to Janssen's *Remicade* (infliximab). It is approved for rheumatoid arthritis, ulcerative colitis, psoriasis, psoriatic arthritis, ankylosing spondylitis, and Crohn's disease (adult and pediatric). Launch was expected this month, but litigation could delay this, said Tharaldson.
- Sandoz's *Erelzi* (etanerceptszzs), approved in August 2016. This is a non-interchangeable biosimilar to Amgen's Enbrel (etanercept). It is approved for rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, and juvenile idiopathic arthritis. Launch is possible in February 2017, but it's likely to be delayed, said Tharaldson.
- Amgen's *Amjevita* (adalimumabatto), approved in September 2016. This is a non-interchangeable biosimilar to AbbVie's *Humira* (adalimumab). It is approved for rheumatoid arthritis, psoriasis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis and juvenile idiopathic arthritis. It could be launched in March 2017, but will likely be delayed, said Tharaldson.
- There are also several biosimilars currently pending approval, said Tharaldson. They are: *Filgrastim* (Grastofil, Apotex);

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In Brief . . .

- **China Resources Pharmaceutical Group** will launch an initial public offering aimed at raising between HK$13 billion and HK$15.6 billion (US$1.68 billion-US$2.0 billion.) Sources close to the plan stated that approximately 50% of the offer will be sold to cornerstone investors, with shares ranging between HK$8.45 and HK$10.15 (US$1.09 – US$1.31).
- The completion of the merger between **Quintiles Transnational Holdings** and **IMS Health** was announced on October 10th. In a statement, Quintiles CEO, Tom Pike, said "This combination addresses life-science companies' most pressing needs: to transform the clinical development of innovative medicines, demonstrate the value of these medicines in the real world, and drive commercial success. We are bringing together two best-in-class leaders. I'm confident that together we will make our clients even more successful." The new company name is **QuintilesIMS**. Shares of IMS stock was converted into 0.3840 shares of Quintiles stock.
- **Profarma** (Brazil) has acquired the chain **Rosário**, nearly doubling the Group's retail presence. Approximately 280 stores will be distributed throughout the southeast and Midwest regions of Brazil, contributing to Profarma's efforts to further integrate companies and capture valuable market share. The deal was valued at R$173 million (US$54.02 million), and faces approval by the Brazilian Antitrust Authority.
- **Sinopharm**, China's largest state-owned pharmaceutical group, has submitted a second draft of its mixed ownership reform plan to the Stateowned Assets Supervision and Administration Commission. This move will further increase the power of its board of directors as part of the company's mixed ownership reform process. Second submissions are normal practice and may require more details in the future, if so directed by the SASAC. Sinopharm is one of six state-owned enterprises that have been selected to pilot reforms in ownership, management and supervision.

(Sources: China Daily, Drug Store News, Reuters, Press Releases)

U.S. DEA Reducing Schedule II Drug Production

(Sources: U.S. Drug Enforcement Administration and Centers for Disease Control and Prevention)

The United States Drug Enforcement Administration (DEA) has reduced the amount of almost every Schedule II opiate and opioid medication that may be manufactured in the United States in 2017 by 25% or more, according to a Final Order published in the Federal Register earlier this month. A handful of medicines were reduced by more, such as hydrocodone, which will be 66% of last year's level. Demand for these opioid medicines, represented by prescriptions written by DEA-registered practitioners, has decreased according to sales data obtained by DEA from IMS Health, which provides insurance companies with data

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Trends (cont.) . . .

Pegfilgrastim (Apotex); *SB2 infliximab* (Merck/Samsung Bioepis); *CHS-1701*, a pegfilgrastim (Coherus Biosciences); *Epoetin alfa* (Retacrit, Pfizer);

4. Cancer drug development is a key focus area. About 1.7 million cases of cancer are diagnosed each year in the U.S. Still, the cancer death rate has fallen 23% since the early 1990s, due to a drop in smoking, better and earlier diagnosis, and new medications and treatments, said Tharaldson. The "development of cancer medications is very extensive," she said, noting that in the last year, 15 new cancer medications were approved. Though not as many are likely to be approved this year, Tharaldson said the trend toward more cancer medications will continue;

5. Orphan drug development will continue to expand. There are approximately 7,000 orphan diseases affecting 30 million patients in the U.S., said Tharaldson, noting that these medications are extremely expensive. "About 40% of the specialty pipeline is focused on orphan medications," she said. When orphan medications and cancer medications are combined, they make up about two-thirds of the specialty pipeline.

DEA (cont.) . . .

on prescriptions written and prescription medications sold in America.

The Aggregate Production Quota (APQ) established by the Final Order is the total amount of a controlled substance necessary to meet the estimated medical, scientific, research, industrial, and export needs for the year and for the maintenance of reserve stocks. The 2017 APQ has been reduced for *oxycodone*, *hydrocodone, fentanyl, hydromorphone, morphine*, and other such medications. Much of this reduction is attributed to the elimination of a 25% buffer that was added to the APQ annually in 2013 through 2016 to guard against shortages.

The *2015 National Survey on Drug Use and Health* (NSDUH) released last month found 6.5 million Americans over the age of 12 used controlled prescription medicines non-medically during the past month, second only to marijuana and more than past-month users of cocaine, heroin, and hallucinogens combined.

Earlier this year the Centers for Disease Control and Prevention (CDC) issued guidelines to practitioners recommending a reduction in prescribing opioid medications for chronic pain. For years, DEA and others have been educating practitioners, pharmacists, manufacturers, and the public about the potential dangers of the misuse of opioid medications.

When the U.S. Congress passed the Controlled Substances Act (CSA), the quota system was intended to reduce or eliminate diversion from "legitimate channels of trade" by controlling "the quantities of the basic ingredients needed for the manufacture of [controlled substances]." The purpose of quotas is to provide for the adequate and uninterrupted supply for legitimate medical need of the types of schedule I and II controlled substances that have a potential for abuse, while limiting the amounts available to prevent diversion. DEA establishes APQs for more than 250 Schedule I and II controlled substances annually.

In setting the APQ, DEA considers data from many sources, including estimates of the legitimate medical need; estimates of retail consumption based on prescriptions dispensed; manufacturers' data on actual production, sales, inventory, exports, product development needs, and manufacturing losses; data from DEA's own internal system for tracking controlled substance transactions; and past quota histories. Once the aggregate quota is set, DEA allocates individual manufacturing and procurement quotas to those companies that apply for it. DEA may revise a company's quota at any time during the year if change is warranted due to increased sales or exports; new manufacturers entering the market; new product development; or product recalls.

From 2000 to 2014 nearly half a million Americans died from drug overdoses. Opioid overdose deaths, including both opioid pain relievers and heroin, hit record levels in 2014, with an alarming 14% increase (47,000 deaths) in just one year, according to new data published in CDC's Morbidity and Mortality Weekly Report.

The most commonly prescribed opioid pain relievers, those classified as natural or semi-synthetic opioids such as oxycodone and hydrocodone, continue to be involved in more overdose deaths than any other opioid type. These deaths increased by 9% (813 more deaths in 2014 than 2013).

Increases in prescription opioid pain reliever and heroin deaths are the biggest driver of the drug overdose epidemic. Deaths from heroin increased in 2014, continuing a sharp rise that has seen heroin overdoses triple since 2010. Deaths involving illicitly made fentanyl, a potent opioid often added to or sold as heroin, also are on the upswing.

"The increasing number of deaths from opioid overdose is alarming," said CDC Director Tom Frieden, M.D., M.P.H. "The opioid epidemic is devastating American families and communities. To curb these trends and save lives, we must help prevent addiction and provide support and treatment to those who suffer from opioid use disorders. This report also shows how important it is that law enforcement intensify efforts to reduce the availability of heroin, illegal fentanyl, and other illegal opioids."

Drug overdose deaths are up in both men and women, in non-Hispanic whites and blacks, and in adults of nearly all ages. Rates of drug overdose deaths were highest among five states: West Virginia, New Mexico, New Hampshire, Kentucky, and Ohio.

The findings show that two distinct but intertwined trends are driving America's overdose epidemic: a 15-year increase in deaths from prescription opioid pain reliever overdoses as a result of misuse and abuse, and a recent surge in illicit drug overdoses driven mainly by heroin. Both of these trends worsened in 2014.

More than six out of 10 drug overdose deaths in 2014 involved opioids, including opioid pain relievers and heroin. The largest increase in opioid overdose deaths involved synthetic opioids (not including methadone), which were involved in 5,500 deaths in 2014, nearly twice as many as the year before. Many of these overdoses are believed to involve illicitly-made fentanyl, a short-acting opioid.

In addition, heroin-related death rates increased 26% from 2013–2014, totaling 10,574 deaths in 2014. Past misuse of prescription opioids is the strongest risk factor for heroin initiation and use—especially among people who became dependent upon or abused prescription opioids in the past year. The increased availability of heroin, its relatively low price (compared to prescription opioids), and high purity appear to be major drivers of the upward trend in heroin use, overdoses, and deaths.