MRx
TREND ALERT
NOVEMBER 2017 | VOLUME 4, ISSUE 4
YOUR QUARTERLY SOURCE FOR KEY TRENDS

INSIDE THIS ISSUE

AMAZON PRIME PHARMACY?

Over the past few years, Amazon, Netflix, and Hulu have disrupted the television world with on-demand programming, much to the astonishment of network television. Prime programming is only a small part of Amazon's offerings. Along with their traditional home goods products, the powerhouse online retailer has a variety of other services ranging from grocery delivery to music streaming, with various memberships for several target demographics. Amazon always seems to be on the cutting edge, whether it is an acquisition of a large health-focused grocery chain, nearly immediate delivery, or talk of drone technology for transporting goods. Now, there is buzz that Amazon may enter the pharmacy arena.

Many say it is inevitable that Amazon will have a role in the pharmacy space; it is not a matter of if, but when. Nonetheless, the position Amazon will play in that space poses a number of questions. Amazon has acquired a wholesale drug distribution license in at least 12 states. This would allow Amazon to serve as a wholesaler, but additional licensing or partnerships would be required for other functions in the drug supply chain. What are some of these possible speculated roles? Amazon could simply serve as a mail-order retailer for medications, devices, and/or medical supplies. Perhaps with their recent grocery acquisition, they may pursue select brick and mortar pharmacies. Or, playing an even larger part, they could negotiate independently with pharmaceutical companies, serving a function more similar to a pharmacy benefits manager, with impact on drug prices. Amazon could also partner with a specialty pharmacy, targeting the rapidly growing specialty spend. While there are many possibilities, the exact role and timing remains unknown. Should Amazon enter the pharmacy space, the effects would not be immediate; it could take many months to obtain the appropriate licensing in all states.

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Despite the fact that "Amazon Pharmacy" is still speculation, the effects have been evident. Select retailers, wholesalers, and pharmacy benefit managers have seen share values fall amid uncertainty and reports of wholesale license procurements. CVS Health Corp. is in negotiations to purchase Aetna Inc., a move to expand and solidify their footprint in the pharmacy world and thought to be partially related to the squeeze from the Amazon frenzy. Likely also a pre-emptive move, CVS announced nationwide next-day and same-day delivery in select areas beginning in 2018. Dubbed the "Amazon effect," the rumors alone have already disrupted the pharmacy space, leaving some key pharmacy players feeling a lot like network television. ■

KEEP ON YOUR RADAR: MOTHER NATURE AND DRUG SHORTAGES

Harvey, Irma, Jose, and Maria. Sound familiar? Unfortunately, 2017 has been 1 of the busiest tropical storm seasons on record, dealing catastrophic devastation to human life, homes, infrastructure, and survival basics. In September, Hurricane Maria, a Category 4 storm, blew in with 150 mph winds causing a major humanitarian crisis in the U.S. Territory of Puerto Rico (PR). By late October, only 25% of electricity service had been restored to the island, and initial assessments indicate that it might be months before all of PR's power will be restored.

One of the concerns in the aftermath of the storm is the potential for drug shortages. PR is home to a $15 billion pharmaceutical industry because of tax incentives created decades ago. This island territory provides nearly 10% of all drugs used in the U.S., and more than 50 medical device plants operate in PR. A comprehensive list of the products made in PR factories has not been released, but the U.S. Food and Drug Administration (FDA) is watching 40 products for shortages, 14 of which are sourced exclusively out of PR. The anti-rheumatic drug Humira®, the oral anticoagulant Xarelto®, and even Tylenol® are among the drugs being monitored. The FDA is working closely with approximately 10 device companies who may be the sole manufacturer of a device and whose products may be life-sustaining. Due to the hurricane, reduced supplies of select surgical staples and orthopedic surgery products have been shipping to U.S. hospitals. Strategies employed by the FDA to mitigate shortages include working with local and federal regulators, as well as manufacturers, to provide diesel fuel, manufacturing supplies, and logistical support, such as relocating critical products off the island. The FDA facilitated importation of saline mini-bags, a routinely used intravenous (IV) fluid that is still in shortage in U.S. hospitals. Review and approval of select generics and dosage forms have also been expedited and surrogate facilities permitted for production, as an alternate means for access to some of these life-saving medications.

Almost 2 months after the behemoth storm, the island is hobbled by shortages of electricity, water, and damages sustained to daily living affecting the workforce. Mother Nature has blown in an immediate and potentially long-term impact on product availability. Drug price gouging has even been speculated as 1 of the long-term debris of the hurricane. The duration to full recovery will be the barometer for the broader context of the drug and device supply chain to be realized. ■

DID YOU KNOW? FDA INITIATIVES – ORPHAN DRUGS, ABUSE-DETERRENT OPIOIDS, AND GENERIC COMPETITION

In May 2017, Scott Gottlieb, M.D., was announced as the new Commissioner of the FDA. Under new leadership, the FDA has unveiled several new initiatives.

One of their initiatives is a plan aimed to reduce the backlog of Orphan drug designation requests, known as the Orphan Drug Modernization Plan. Orphan drug designation, which is generally defined as a drug used for diseases affecting fewer than 200,000 people in the U.S., provides various incentives for the drug sponsor. At the time of the announcement in June, the FDA had approximately 200 Orphan drug designation requests pending review and, based on recent trends, were anticipating this number to grow. Within the plan, the FDA has a "90 in 90" goal to address all requests older than 120 days within 90 days and subsequent requests within 90 days of submission. The first part of this goal has been achieved. In addition, the FDA has announced a continued dedication to modernize stewardship of Orphan drug designation intent.

Also in June, the FDA announced new steps to assess opioids with abuse-deterrent properties and other opioid issues, with Dr. Gottlieb citing this as his highest public health priority. A public meeting, held in mid-July, examined whether the FDA's current method of assessing abuse-deterrence properties is the best way to determine what measures are most likely to limit misuse. To guide the discussion, the FDA created an Issues Paper to identify select challenges in the development of abuse-deterrent formulations, including identification of appropriate outcomes, measures, and study designs. Since then, they have sought expert advice on abuse-deterrence and encouraged the safe use of medication-assisted treatment. It was also announced that the FDA is investigating the potential benefit of mandatory healthcare provider opioid education and evaluating opioid packaging, storage, and disposal. In October, Dr. Gottlieb announced 3 additional steps the FDA is taking: (1) guidance for addiction treatment product development; (2) promotion of more widespread use of FDA-approved therapies; and (3) efforts to reduce the stigma associated with addiction treatment.

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The FDA also recently announced the Drug Competition Action Plan, designed to indirectly curb the costs of drugs by reducing barriers to generic drug approval. The FDA announced their plan to release 2 guidance documents to improve the generic approval process, 1 to internally steer stringent and consistent evaluation and communication and 1 to provide advice on how to avoid common filing deficiencies. In addition, the FDA plans to expedite the review for abbreviated new drug applications (ANDAs) with reference products that have fewer than 3 approved generics and published a list of branded agents that currently have no approved generics.

Several other targets have been identified by the FDA, including reiterating its focus to oversee the safety of compounded drugs, patient engagement, medical device innovation, stem cell therapies, and adverse event reporting. With new leadership comes a new focus from the agency. These last 6 months have offered a glimpse of the upcoming objectives of the FDA. ■

MEDICAL PHARMACY CORNER

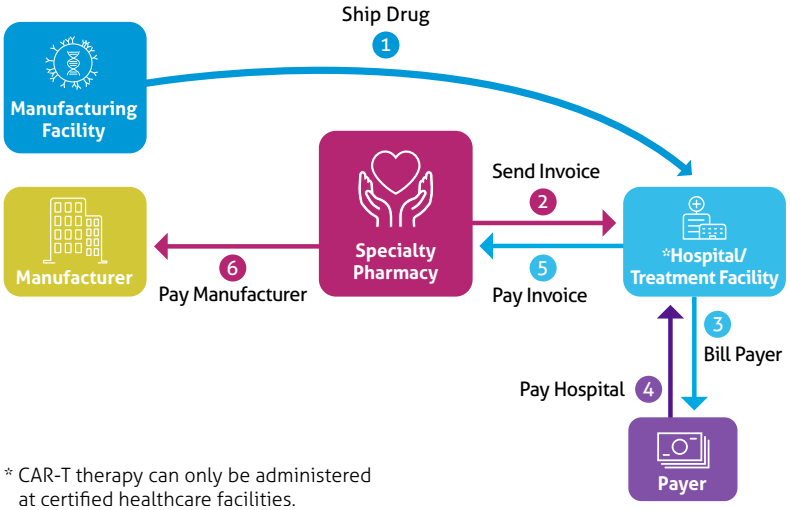
CHIMERIC ANTIGEN RECEPTOR-T CELLS (CAR-T): A UNIQUE REVENUE CYCLE FOR A UNIQUE THERAPY

There are now 2 FDA-approved CAR-T therapies, tisagenlecleucel (Kymriah™) and axicabtagene ciloleucel (Yescarta™). As described in a prior edition of the MRx Trend Alert, these products are live cell therapies, different from traditional drugs and biologics. They start with T cells being apheresed from the patient and shipped to the manufacturer for genetic modification. The CAR-T cells are then returned for patient-specific reinfusion. This new drug delivery channel differs from the current standard approach for most drugs and biologics where drugs are shipped from the manufacturer to a wholesaler who physically distributes the medication to a pharmacy. Therefore, the chain of command is critical with CAR-T therapies to ensure the patient is correctly reinfused with only their own personal genetically modified T cells.

Another unique aspect of this "living drug" therapy is that the genetically modified T cells returned to the treating facility will be handled by laboratories rather than having the drug dispensed through the institution's pharmacy department. Since the institution's laboratory will be the "dispensing" discipline, the traditional charge and billing system typically performed by the pharmacy department will be absent. To compensate for this lack of functionality, both Novartis (Kymriah) and Kite/Gilead (Yescarta) have elected to utilize a specialty pharmacy to handle this process. The role of the specialty pharmacy will be limited to processing the billing, as these specialty pharmacies will never handle the actual CAR-T preparation. As depicted in Figure 1, the specialty pharmacy invoices the hospital/treatment facility when the CAR-T cells are delivered back to the facility and, in turn, pays the manufacturer after collecting payment from the payer. Potential further complexities to this revenue cycle include manufacturer agreements with the treatment facilities. These agreements ensure that the facilities will not be held financially responsible if the patient is unable to receive the product due to a change in the patient's clinical condition. It has also been reported that Novartis may be entering into an outcomes-based contract with the Centers for Medicare & Medicaid Services (CMS) that would allow CMS to forgo payment for the CAR-T preparation if the patient has not had a response to Kymriah by the end of the first month.

CAR-T therapies are an innovative treatment for refractory malignancies, which also require new processes to be developed in terms of revenue cycles. Given the high cost of these therapies, it is imperative for all participants to ensure that billing and reimbursement procedures are streamlined and adaptable to account for potential complexities, including manufacturer agreements and outcomes-based pricing. ■

Figure 1. CAR-T Invoicing Flowchart



* CAR-T therapy can only be administered at certified healthcare facilities.

PIPELINE REPORT: 4TH QUARTER 2017/1ST QUARTER 2018

DRUG MANUFACTURER	CLINICAL USE	ANTICIPATED DATE	PROJECTED MARKET IMPACT
Select Branded Pipeline Agents: Potential New Emerging Expenses for Health Plans			
semaglutide Novo Nordisk	Type 2 diabetes mellitus	December 5, 2017	Second subcutaneous glucagon-like peptide-1 (GLP-1) agonist with cardiovascular risk reduction data; will compete with the market leader liraglutide (Victoza®)
voretigene neparvovec Spark	Inherited retinal disease	January 12, 2018	Intraocular adeno-associated virus (AAV)-derived gene therapy vector for biallelic *RPE65*-mediated retinal disease; may be first option to improve functional vision, light sensitivity, and visual field in these patients; Breakthrough therapy/Orphan drug/Priority review
andexanet alfa Portola	Anticoagulant reversal	February 2, 2018	First universal reversal agent targeting direct and indirect factor Xa inhibitors, including apixaban (Eliquis®), edoxaban (Savaysa®), rivaroxaban (Xarelto), and enoxaparin (Lovenox®); IV; Breakthrough therapy/Orphan drug/Priority review
bictegravir/ emtricitabine/ tenofovir alafenamide (TAF) Gilead	HIV-1 infection	February 12, 2018	Oral fixed-dose product for HIV-1 infection containing a next-generation integrase strand inhibitor (INSTI), which does not require "boosting" with another drug to prolong levels in the body, in combination with 2 nucleoside reverse transcriptase inhibitors (NRTIs); likely to compete with GlaxoSmithKline's Triumeq® (abacavir/ dolutegravir/TAF); Orphan drug/Priority review
Select New Generics/Patent Expirations			
efavirenz tablets generic for Bristol-Myers Squibb's Sustiva®	HIV-1 infection	December 2017	Settlement agreement; Mylan eligible for 180-day exclusivity; U.S. sales of $137 million in 2016
tenofovir disoproxil fumarate tablets and powder generic for Gilead's Viread®	HIV-1 infection	December 15, 2017; January 26, 2018	Settlement agreement for 300 mg tablets, expected in December; other tablet strengths and powder expected in January following pediatric exclusivity expiration; U.S. sales of at least $833 million in 2016
atazanavir sulfate capsules generic for Bristol-Myers Squibb's Reyataz®	HIV-1 infection	December 27, 2017	Settlement agreement; Teva eligible for 180-day exclusivity; U.S. sales of $558 million in 2016
Select Biosimilars			
Truxima – biosimilar to Genentech's Rituxan® Celltrion/Teva	Non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, granulomatosis with polyangiitis, and microscopic polyangiitis	1Q 2018	IV CD20-directed cytolytic antibody; biosimilar for rituximab; product launch likely to be delayed due to regulatory hurdles; Rituxan (rituximab) had U.S. sales of $3.99 billion in 2016

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