MRx TREND ALERT

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YOUR QUARTERLY SOURCE FOR KEY TRENDS

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DID YOU KNOW? STATES TAKE ON RISING DRUG PRICES

Rising drug costs have received a great deal of attention recently. For anticancer drugs in particular, recent data has demonstrated that both the initial launch price point and the subsequent rate of price increases after launch have accelerated over the last decade.

California (CA) became one of the first states to pass a sweeping law aimed at curbing these price increases and increasing their transparency. The CA law applies to any prescription drug exceeding a wholesale acquisition cost (WAC) of $40 for a course of therapy and, therefore, is quite broad in scope. Manufacturers are required to give 60-day notice if the WAC rises more than 16% over a 2-year period. Another aspect of the law, which will not go into effect until 2019, mandates that manufacturers report detailed information about these price increases to a state governmental agency. For drugs that exceed the 16% WAC increase over 2 years, the manufacturer will be required to report the financial and nonfinancial factors impacting the decision around the price increase. Furthermore, state agencies will be required to compile an annual report that demonstrates the overall impact of drug costs on healthcare premiums.

Critics of the law say there is no evidence that it will lower drug costs for patients and does not provide full transparency since it does not include rebate information. Despite these concerns, other states have passed similar, but less sweeping, legislation. Nevada's law focuses solely on pricing transparency for drugs used to treat diabetes and requires data to be reported from manufacturers, sales representatives, pharmacy benefit managers (PBMs), and select nonprofit organizations. Vermont's (VT) drug price transparency legislation focuses on the top 15 drugs for which the state spends "significant healthcare dollars." It requires manufacturers with price increases of ≥ 50% over the past 5 years or ≥ 15% over the past 12 months to report information on pricing. The findings are then reviewed by state officials and posted to the VT Attorney General's website. Maryland passed a law prohibiting "price gouging" of generic drugs as well as any drug with WAC price increases of ≥ 50% from the preceding 1-year period. Litigation is currently ongoing around several of these state laws.

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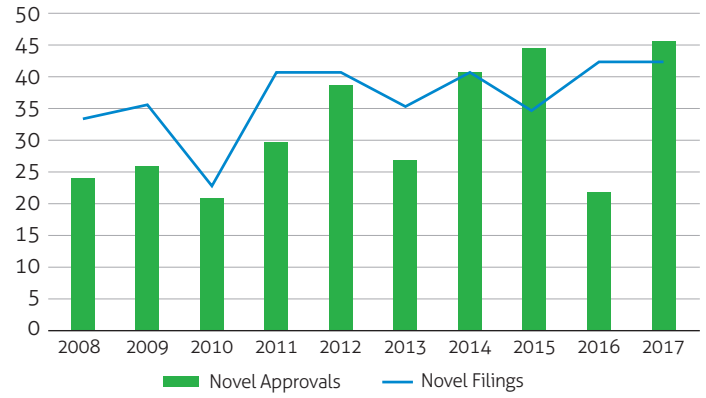
Multiple stakeholders, including state governments, continue to grapple with how to best address the rising cost of pharmaceuticals. Ultimately, the issue may be partially answered by the national shift in focus to value-based care. ■

FDA APPROVALS: A YEAR IN REVIEW

In January, the Food and Drug Administration's (FDA) Center for Drug Evaluation and Research (CDER) published *Advancing Health through Innovation: 2017 New Drug Therapy Approvals.* This report provides a benchmark for approvals and highlights the game-changers approved in 2017. Compared to 2016, in which CDER only approved 22 new drugs, 46 novel agents were approved in 2017, which does not even include the first gene therapy for an inherited retinal disease and 2 landmark chimeric antigen receptor T-cell (CAR-T) therapies. This marks the largest number of novel approvals in over 2 decades and far exceeds the average of 31 novel approvals per year in the past 10 years. Figure 1 outlines approvals and filings over the past 10 years.

Figure 1. Novel New Drug Approvals by Year



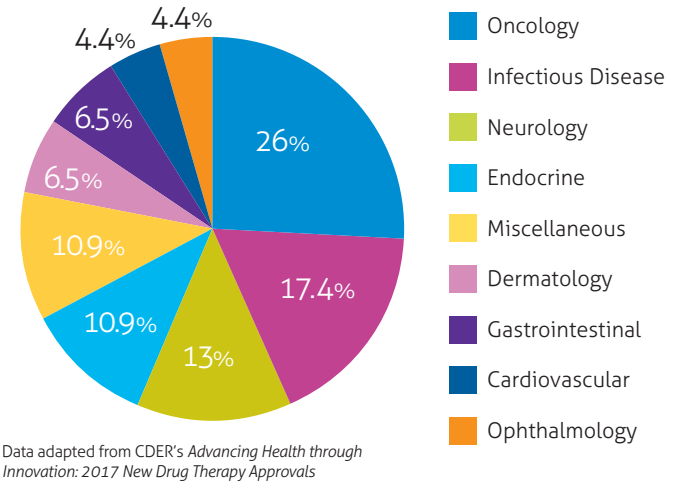
Data adapted from CDER's *Advancing Health through Innovation: 2017 New Drug Therapy Approvals*

*2017 filing data as of 11/30/2017

Several potential explanations may account for this increase. The FDA was operating under new leadership with new strategic initiatives, and Congress enacted potentially impactful legislation (e.g., the 21st Century Cures Act). Public interest in the opioid crisis and drug shortages have also put the FDA on the forefront of the public's mind, further challenging the FDA to demonstrate action in the public's interest. Moreover, the FDA received some criticism in early 2017 following the lower than average approvals in 2016.

Last year, all 46 novel drug approvals met their Prescription Drug User Fee Act (PDUFA) goal dates. In 2017, 33% were considered first-in-class and 39% were approved for rare diseases (Orphan drugs). Priority review was granted to 61% of new drugs, 13% received Accelerated approval, 39% garnered Fast track designation, and 37% were designated as Breakthrough therapy. In addition, 85% were approved in the first review cycle, and 78% were approved in the US prior to approval in other countries. A breakdown of the types of drugs approved in 2017 is illustrated in Figure 2. ■

Figure 2. Drug Approvals by Class



Data adapted from CDER's *Advancing Health through Innovation: 2017 New Drug Therapy Approvals*

KEEP ON YOUR RADAR: THE 4TH INDUSTRIAL REVOLUTION – DIGITAL THERAPEUTICS

The 4th Industrial Revolution has arrived and is fundamentally transforming how we live, work, and connect. Fueled with a digital engine, robotics, artificial intelligence, voice-enabled devices, wearables, and autonomous cars are accelerating at an unprecedented rate and disrupting almost every industry. The medical field is no exception.

The digital revolution has given birth to digital therapeutics (DTx) or digiceuticals, a global market expected to be worth upwards of $9 billion by 2025. Using digital platforms such as mobile apps and software, this new class of medicine helps treat and prevent diseases by modifying patient behavior and providing remote monitoring to improve long-term health outcomes. DTx can either augment conventional medications or replace them. The key difference between DTx and general wellness apps that have proliferated on the market is that DTx is tailored to specific diseases. DTx targets chronic conditions with a central role of patient behavior in preventing and limiting disease severity (e.g., diabetes, hypertension, mental health). The data from these mobile-delivered solutions have the potential to empower patients to make better decisions about their own health, improve adherence, arm healthcare teams with insight into patient behavior, and lead to improved outcomes. The scalable, lower-cost nature of DTx, and earlier intervention in the disease spectrum, lends itself to potential cost savings and value in a collaborative care model.

Outcomes to show DTx as a clinically validated digital health solution will be central to securing insurance coverage. Regulatory framework is advancing forward as the FDA creates digital guidance and oversight, including a third-party pre-certification DTx pilot for apps in development that has been likened to a Transportation Security Administration pre-check. A new industry association, the Digital Therapeutics Alliance (DTA), also has been formed by health startups to advance DTx.

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In late 2017, Abilify Mycite® (aripiprazole) made headlines as the first FDA-approved digital pill for schizophrenia. Embedded with an ingestion-tracking device that is activated once inside the body, it communicates with an app through a transdermal patch, providing data to the patient. Abilify Mycite, which has not been shown to increase adherence, raises ethical questions about DTx. Questions regarding patient privacy, data liability, and whose responsibility it is to intervene to ensure appropriate use are among the sensitive boundaries to consider for DTx's long-term success.

Digital therapeutics is here. Given the average American touches his/her smartphone about 2,617 times per day, the implications of DTx are vast! Stakeholders have a collective opportunity to shape its future. Are you ready? ■

MEDICAL PHARMACY CORNER

BIOSIMILARS – A SLOW START OUT OF THE GATE?

Biologic drugs are large, complex molecules manufactured in living organisms and are an important treatment modality for a wide range of diseases. Biologic drugs are more complicated and difficult to manufacture than traditional, small molecule drugs, and constitute some of the most costly drugs on the market. Many biologicals are not suitable for self-administration and instead are often administered in a provider office or clinic. As such, they are covered under Medicare Part B for Medicare recipients. In 2015, biologics accounted for the majority (65%) of Medicare Part B spending, totaling $26 billion.

Biosimilars are drugs deemed by the FDA to be "highly similar" and have "no clinically meaningful differences" from the original (reference) biologic. To date, the FDA has approved 9 drugs through the biosimilar pathway, but only 3 of them are currently commercially available with uptake slower than predicted. The reasons for the slower than anticipated adoption of biosimilars are multifactorial and include the lack of clinical experience with biosimilars, legal hurdles, and pricing issues.

The launch price for marketed biosimilars has ranged from approximately a 15% to a 35% discount compared to the list price of the reference biologic. Despite this discount, some private payers are still incentivized to promote usage of the reference biologic due to more favorable contract pricing. The payer may be able to achieve a lower net price for the reference biologic than the biosimilar despite the lower list price of the biosimilar.

In 2016, the Centers for Medicare and Medicaid Services (CMS) stipulated all biosimilar products for a particular reference biologic would have a single billing and payment code. Medicare reimbursement for biosimilars would use a blended average sales price (ASP) of all the biosimilars within the same Healthcare Common Procedure Coding System (HCPCS) code or J-code. Reimbursement would be calculated as the blended ASP of all the biosimilars within a single HCPCS code plus 6% of the ASP of the reference biologic. Many stakeholders were opposed to this 2016 CMS ruling; some argued the combined HCPCS code reimbursement structure would decrease manufacturer incentives for biosimilar development and ultimately increase Medicare costs. Based on comments solicited by CMS regarding the impact of the policy, CMS has announced changes. Effective January 1, 2018, each biosimilar will be assigned its own unique HCPCS code and reimbursement will be based on the ASP of the individual biosimilar plus 6% of the reference biologic's ASP. CMS expects this policy change will encourage greater manufacturer participation in the marketplace and lead to the introduction of more biosimilars, possibly leading to long-term cost savings for Medicare and its beneficiaries.

Many complicated clinical and market dynamics have thus far restricted the widespread uptake of biosimilars. However, analysts still predict that eventually biosimilars will produce cost savings either due to increased biosimilar utilization or perhaps by slowing the rate of biologics' pricing increases. ■

PIPELINE REPORT: 1ST AND 2ND QUARTER 2018

DRUG MANUFACTURER	CLINICAL USE	ANTICIPATED DATE	PROJECTED MARKET IMPACT
Select Branded Pipeline Agents: Potential New Emerging Expenses for Health Plans			
tildrakizumab Merck	Plaque psoriasis (PSO)	March 2018	Subcutaneous (SC) interleukin (IL)-23 antagonist; likely to compete directly with guselkumab (Tremfya®) and other IL inhibitors for PSO
ibalizumab Theratechnologies	HIV-1 infection (multidrug resistant)	April 3, 2018	Injectable anti-CD4 antibody (entry inhibitor); Breakthrough therapy; Fast track; Orphan drug; Priority review
burosumab Ultragenyx	Familial hypophosphatemia	April 17, 2018	Intravenous (IV) recombinant human fibroblast growth factor inhibitor; Breakthrough therapy; Fast track; Orphan drug; Priority review
fostamatinib Rigel	Immune thrombocytopenic purpura	April 17, 2018	Oral spleen tyrosine kinase (SYK) inhibitor; Orphan drug
andexanet alfa Portola	Reversal of Factor Xa inhibitor anticoagulation	May 4, 2018	IV modified human protein designed to function as a Factor Xa decoy to reverse the anticoagulant activity of Factor Xa inhibitors; Breakthrough therapy; Orphan drug
elagolix Abbvie	Endometriosis with associated pain	May 6, 2018	First oral gonadotropin-releasing hormone (GnRH) antagonist for women with endometriosis; Priority review
erenumab Amgen	Migraine prevention	May 17, 2018	SC calcitonin gene-related peptide (CGRP) receptor inhibitor; new class for migraine prophylaxis
Select New Generics/Patent Expirations			
hydroxyprogesterone caproate generic for AMAG's Makena®	Preterm labor	1H 2018	Orphan drug exclusivity expiration; AMAG expected to launch authorized generic at time of FDA-approved generic launch; US sales of $219 million in 2016
memantine HCl extended-release generic for Allergan's Namenda XR®	Alzheimer's disease	February 2018	Settlement agreement; several generic manufacturers expected; US sales exceeding $1.1 billion in 2016
cinacalcet HCl generic for Amgen's Sensipar®	Hyperparathyroidism; hypercalcemia	March 8, 2018	Patent expiration; several generic manufacturers expected; US sales of $1.52 billion in 2016
ethinyl estradiol/ etonogestrel generic for Merck's NuvaRing®	Contraception	April 8, 2018	Patent expiration; several generic manufacturers expected; US sales of $773 million in 2016