2018: Pipeline Year in Review
Key Drug Launches and Approvals

CVS Health
By almost any standard, 2018 was a banner year for U.S. drug approvals.

The U.S. Food and Drug Administration (FDA) approved 59 novel drugs and therapeutic biologics last year — breaking its previous record of 53, set in 1996, according to the “2018 New Drug Therapy Approvals,” from the Center for Drug Evaluation and Research.¹

One-third of the approvals were for first-in-class medications, including the first monoclonal antibody for HIV (ibalizumab-uiyk/Trogarzo) and the first non-opioid drug to treat the symptoms of opioid withdrawal (lofexidine hydrochloride/Lucemyra). More than half were for rare or orphan diseases, including new treatments for phenylketonuria (pegvaliase-pqpz/Palynziq) and a rare form of rickets that does not respond to treatment with vitamin D (burosumab-twza/Crysvita). Fourteen were designated as Breakthrough Therapies. Oncology alone saw 16 new drug approvals.

What makes a good year in drug development, of course, is not just the number of drugs approved, but the specifics of individual drugs and groups of drugs and the impact they may have on the quality of patients’ lives and on prescription drug spending in the nation. In previous Insights, we have discussed several key approvals, including the new expanded indication for Hemlibra (emicizumab), which permits the breakthrough hemophilia drug to be used in all hemophilia patients of all ages regardless of whether they have developed inhibitors. We also highlighted Epidiolex, a treatment for two rare and life-threatening forms of epilepsy, and the agency’s first approval for a drug based on cannabidiol, a key compound in cannabis.

Here are some noteworthy recent approvals and therapies that could come up for FDA consideration over the next few months.

Preventing Migraine

Three new medications intended to prevent migraine headaches have been approved, with a fourth awaiting FDA action.² The new drugs — Ajovy (fremanezumab), Emgality (galcanezumab), and Aimovig (erenumab) — are all injectables that work by blocking the activity of calcitonin gene-related peptide (CGRP), a substance that helps neurons communicate with each other and is seen at elevated levels during migraine. The drugs are the first to be developed specifically to prevent migraine; other drugs in the category were originally developed to treat other conditions such as high blood pressure. In clinical trials patients showed a wide range of response to CGRP inhibitors, with some experiencing only modest effects, while others showed dramatic improvement.

New Hope for Uncontrolled Asthma

Not all of 2018’s most significant approvals were for novel drugs. Dupixent (dupilumab), for instance, was originally approved in 2017 as a treatment for moderate to severe atopic dermatitis not adequately controlled by topical therapies.³ Its latest approval is as an add-on maintenance treatment for patients aged 12 and older with two types of moderate-to-severe asthma: asthma marked by elevated levels of a type of white blood cells called eosinophils, and asthma in which long-term treatment with corticosteroids interferes with the adrenal gland’s ability to produce corticosteroids on its own as needed (“oral corticosteroid dependent asthma”). The drug is an injectable monoclonal antibody that targets two receptors of the signaling protein interleukin, which plays a role in inflammation.⁴

Manufacturers Sanofi and Regeneron have filed for approval to use Dupixent for nasal polyps and have announced trials to test the drug in a variety of other conditions, including pediatric asthma and several forms of allergy.⁵
A New Once-a-Day HIV Drug

Biktarvy is a daily HIV tablet combining bictegravir, a new integrase inhibitor, with two nucleoside/nucleotide reverse transcriptase inhibitors: emtricitabine and tenofovir alafenamide, the two active ingredients that make up the HIV therapy Descovy. It has been approved for the treatment of HIV-1 infection in adults not previously treated with antiretrovirals or as a replacement regimen for patients who are virologically suppressed on a stable antiretroviral regimen for at least three months. Biktarvy quickly became the second-most-prescribed HIV medication in the U.S. and is expected to reach sales of more than $5 billion by 2022.

Oncology

Drugs for cancer continued to make up about a quarter of the new therapies approved, and of the 16 new drugs approved last year, 13 were for orphan indications. Notable on the list were:

- **Vitrakvi** (larotrectinib), just the second “tissue agnostic” cancer drug approved by the FDA. The oral drug is indicated for cancers that show a particular biomarker, regardless of location in the body, and in clinical trials was effective in treating a variety of tumors, including soft tissue sarcoma, salivary gland cancer, infantile fibrosarcoma, thyroid cancer, and lung cancer. In an interesting move, the drug’s manufacturer has actually agreed to refund the cost of the therapy if the patient does not respond to it.

- **Erleada** (apalutamide tablets), the first approved treatment for prostate cancer that has not metastasized but continues to grow despite hormone therapy.

- **Libtayo** (cemiplimab-rwlc for IV infusion), the first treatment specifically intended for advanced forms of metastatic cutaneous squamous cell carcinoma (CSCC), the second-most diagnosed skin cancer in the U.S. and a potentially deadly disease.

Some 2019 approvals and launches to watch for include:

- **AR101**
  Aimmune’s oral, peanut-based immunotherapy for peanut allergy. Peanut allergy affects an estimated 2 percent of American children, as well as many adults, and can be life-threatening. Until now, the only approved form of management for peanut allergy was rescue epinephrine, though some allergists have long performed “home brew” immunotherapy using peanut products. Despite delays created by the government shutdown, the drug is still expected to launch before the end of the year.

- **Zulresso** (brexanolone)
  The first drug specifically for post-partum depression, a potentially life-threatening condition that affects roughly 400,000 U.S. women per year. The drug, an injectable, was overwhelmingly endorsed by the FDA’s Psychopharmacologic Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee, and its manufacturer, Sage Therapeutics, currently anticipates a June launch.

- **Spravato** (esketamine nasal spray)
  A fast-acting antidepressant intended for patients for whom current therapies have failed, was just approved by the FDA. The drug is chemically related to the anesthetic (and problematic street drug) ketamine, and has raised a range of concerns including blood pressure problems, the potential for misuse, and dissociation, a temporary mental state in which a person might become less aware of their surroundings. Nonetheless, it is sure to be closely watched as the first of a new generation of antidepressives.

- **Zolgensma** (onasemnogene abeparvovec)
  A gene therapy that replaces the defective gene responsible for spinal muscular atrophy type 1, a deadly neuromuscular disease of infants. Part of the reason to pay attention to Zolgensma is pricing: the drug requires a single intravenous dose, and while the manufacturer has not disclosed the list price for the drug, the company has publicly suggested they would consider a price of up to $5 million as “cost-effective.”
Zolgensma may be the most obvious case, but all of the drugs described here present an array of challenges to payors — challenges that change and evolve with each new therapy that comes to market and each new generic that alters the cost of therapy.

CVS Health constantly monitors the pipeline and proactively develops and implements strategic cost management tools. Prior to launch, we seek input from external thought leaders so that we can model potential impact. We also have dedicated resources including experienced clinicians who closely follow and evaluate the drug pipeline to determine appropriate formulary placement and potential designation as a specialty drug. At launch, new-to-market review and an assessment of clinical appropriateness inform strategic plan design options, such as utilization management, including use of prior authorization, formulary management such as tiered placement, and step therapy requirements.

Troy Brennan, M.D.
Executive Vice President and Chief Medical Officer, CVS Health