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Responding to infectious disease

As this issue of Managed Healthcare Executive® went to press, the COVID-19 pandemic seemed to have been loosening its grip at last. Cases, deaths, hospitalizations — they were all on a downward trend. The Biden administration signaled that we might be entering a new chapter with a change in White House COVID-19 coordinators. Jeff Zients, who has a reputation as a strong, behind-the-scenes manager, was replaced in March by Ashish Jha, M.D., M.P.H., dean of the Brown University School of Public Health, a gifted communicator whose profile has grown during the pandemic because of his strong Twitter game and frequent appearances on television news shows.

COVID-19 has been predictable in its unpredictability. To hedge the bet, wiggle-room words like “seems” and “might” must be used. Fingers are crossed and hovering over the pause button with the news of lockdowns in China.

Even so, it is time to take stock. As our cover story discusses, the notion that we are on a smooth epidemiologic glide path away from infectious diseases and on to chronic ones, such as heart disease and some cancers, has been shattered by the pandemic. And disease outbreaks punctuated the decades prior to COVID-19. The roll call includes West Nile virus, H1N1 flu, Ebola and Zika. Theories about why they are occurring abound. These are viral diseases, and human contact with animals that harbor viruses is increasing. Global travel and trade can light a match to what might have been just a local outbreak, spreading it like wildfire around the world.

We have scientific advances and a strong biotech and pharmaceutical sector to thank for the rapid development of COVID-19 vaccines. But there is also a call for increased investment in public health. Ezekiel Emanuel, M.D., Ph.D., at the University of Pennsylvania, and others envision a public health workforce that would be deployed to battle disease outbreaks. Others have proposed new training programs for “physician-public health practitioners” who could bridge the yawning gap between our hospital-oriented healthcare systems and public health departments and community groups (see page 9). Some experts say improved surveillance for infectious disease, combined with data collection and analytics, would yield the best return on our public health dollars. We should mix and match the best of these and other ideas to give ourselves the best chance of managing future infectious disease outbreaks rather than lurching thoughtlessly from crisis to crisis.

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President and CEO
of MJH Life Sciences®
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Mission Managed Healthcare Executive® provides healthcare executives at health plans and provider organizations with analysis, insights and strategies to pursue value-driven solutions.
In the early 1990s, employers started to carve out prescription drug coverage from the medical benefit. This separation evolved into the pharmacy benefit management (PBM) industry of today. PBMs' landscape focused on managing the cost of the pharmacy benefit and managing drug companies and pharmacies (see chart). PBMs consolidated the purchasing power of employers to obtain rebates from drug companies and discounts for pharmacies.

Over the past several years, a similar development has been occurring with laboratory testing. With the development of thousands of new diagnostic tests, the need for managing the cost of the laboratory benefit is now necessary. Laboratory benefit management (LBM) companies act as an intermediary between laboratory test companies and physicians to manage the use of certain laboratory tests.

What is an LBM?
LBM companies fill the need to manage laboratory testing for payers, which include employers who are self-insured and health insurers. LBM companies that can offer a range of services are gaining influence over clinical lab testing in important ways. They perform several functions, ranging from educating to obtaining prior authorization to setting formularies and determining coverage policies. They also manage claims and the utilization of lab tests, often reviewing medical necessity.

Some payers adopt LBM coverage policies wholesale, whereas others check their own internally developed policies against LBM policies to see whether their own policies might be improved.

Examples of diagnostic tests include the following:

- Molecular gene tests determine the order of DNA building blocks (nucleotides) in an individual's genetic code, a process called DNA sequencing. The purpose of these tests is to identify genetic changes that can cause disease. This is commonly referred to as somatic testing.
- Chromosomal tests analyze whole chromosomes to identify large-scale changes, such as an extra (trisomy) or missing (monosomy) copy of a chromosome, or abnormalities of large segments of chromosomes that underlie certain genetic conditions. This is commonly referred to as germline testing.

Tests are reimbursed according to current procedural terminology codes. Currently, there are approximately 1,860 codes. The price of these tests can vary greatly, ranging between $2,000 and $12,000. The high prices and the number of tests clinicians are ordering can make lab tests a cost burden for payers. As a result, they are seeking ways to better manage the use and reimbursement of such tests. However, the soaring
number of tests is outpacing formularies, billing code sets and clinical utility evidence, which are all necessary for coverage determinations.

Many professional societies have issued guidelines that spell out which tests are medically necessary, but in reality there is minimal adherence to these stated guidelines. In addition, there is just not much agreement on when these tests should be completed.

Today, there often is confusion about which tests get ordered and why. To some extent, the tests physicians order are determined by the pathology laboratories that do the tests. Some are done in-house by the lab, whereas others are sent to an outside lab. Certain payers have said the most efficient use of resources is to have an agreed-upon panel of tests set for each cancer type. The pathology labs are opposed to this practice because it impedes their ability to differentiate their services and may affect their profitability. Labs competing for market share want to be able to control the integrity of their profiling systems from both financial and performance standpoints. That competition can lead to fragmentation.

Payers are also contributing to the chaos. Many have minimal understanding of the evolving technology of genetic testing. They believe that by limiting molecular testing to more traditional methods, as opposed to next-generation sequencing or cell-free DNA technologies, they are controlling cost. Just the opposite may happen. In response to limiting reimbursement to older standards of practice, some laboratories have been known to resort to billing multiple gene codes, also known as stacked billing. As a result, it is not always apparent to the payer whether the tests were appropriate for the patient.

Stuck in the middle are the physicians. They may be knowledgeable about the current recommendation, but labs and payers have turned ordering lab tests into a tug of war. A lab may recommend a test that may be clinically appropriate for the patient, according to current guidelines, and the payer may say the test is not medically necessary, per their coverage policy. But payers also have reason to be wary of unnecessary lab tests ordered because they increase revenues and profits for the labs.

**Do LBMs provide value?**

Both Avalon Healthcare Solutions and Kentmere Healthcare Consulting Corporation state their services can cut the cost of clinical lab testing. Avalon has stated payers can cut costs from between 8% to 12%. Kentmere’s website says health plans can get a 20-to-1 return on their investment.

Several industry associations, such as AHIP, American Medical Association, and Blue Cross Blue Shield Association have reported that LBMs improved genetic test payment turnaround times but also that prior authorization denials have increased.

**Are tests providing value?**

Research generally supports the positive financial impact of genetic testing. The research is largely done on specific diseases. For example, for certain gastrointestinal tumors, studies indicate cost-effectiveness for genetic testing of $92,000 compared with typical treatment regimes. Testing ensures appropriate drug therapy as a part of precision medicine, as well as the avoidance of costly invasive exploratory procedures (e.g., biopsies) that are currently the standard of care.

**Summary**

Although there are differences between PBMs and LBMs, employers can transfer the lessons from one industry segment to another. For the most part, PBMs have provided value to employers in the form of formulary management, utilization management and lower drug costs through volume purchases and rebates. On the flip side, payers acknowledge that PBMs have their limitations and require oversight.

Employers should consider using an LBM to help manage the coverage, reimbursement, claims payment and utilization management of laboratory tests. As the market develops, employers should understand that LBMs provide only a portion of the requirements for better precision medicine and develop strategies to gain a greater benefit.

**Perry Cohen, Pharm.D.**, is CEO of The Pharmacy Group and a member of the Managed Healthcare Executive® editorial advisory board.
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**In Brief**

### ACA enrollment hits record levels

Enrollment in Affordable Care Act (ACA) marketplace plans has reached record levels, and the Biden administration is using those numbers to push for continuation of enhanced subsidies that have lowered premiums for the plans.

CMS announced in March 2022 on the 12th anniversary of the healthcare reform law that enrollment had reached 14.5 million, a 21% increase over last year. About 10 million people enrolled through the federal government’s exchange, Healthcare.gov and the rest through the exchanges that 18 states have set up on their own. Some of the enrollment deadlines for those state-based exchanges are later than the Jan. 15 deadline for Healthcare.gov, so the final tally for the number of Americans in ACA marketplaces is likely to increase.

As a candidate, President Joe Biden said he would build on the ACA rather than push for Medicare for all. The administration has framed the enrollment figures as validation of that approach.

Katie Keith, J.D., M.P.H., an ACA expert who holds positions at the Georgetown University Law Center in Washington, D.C., and writes about the law for *Health Affairs*, noted in a blog post for the journal that enrollment was especially strong in several states that have not expanded their Medicaid programs under the ACA, including Florida, Georgia, North Carolina and Texas.

Keith and the administration pointed to increased subsidies as one of the main reasons for the increased enrollment. About one-third of the people who signed up through Healthcare.gov for coverage selected a plan with a monthly premium of $10 or less. The Biden administration wants the enhanced subsidies to continue and estimates that 3.4 million people will lose coverage through the marketplace plans if they aren’t.

The administration has issued new rules that will apply to the 2023 coverage year. Keith said changes include requirements that seek to standardize benefit design and raise network adequacy standards.

— Peter Wehrwein

### Enrollment in ACA plans

<table>
<thead>
<tr>
<th>Year</th>
<th>Enrollment</th>
</tr>
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<tbody>
<tr>
<td>2018</td>
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</tr>
<tr>
<td>2019</td>
<td>11.4 million</td>
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<tr>
<td>2020</td>
<td>11.4 million</td>
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<tr>
<td>2021</td>
<td>12 million</td>
</tr>
<tr>
<td>2022</td>
<td>14.5 million</td>
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Source: CMS 2022 Open Enrollment Report
Physician-public health practitioners needed

A new kind of specialist is needed at academic medical centers to cope with public health emergencies such as the COVID-19 pandemic, argued the authors of an opinion piece in *JAMA Health Forum* in March. These “physician-public health practitioners” would be trained in how to build partnerships with community organizations, translate scientific information and provide technical assistance to outsider organizations, wrote Kirsten Bibbins-Domingo, Ph.D., M.D., M.A.S., and Alicia Fernandez, M.D., of the University of California, San Francisco, School of Medicine.

As Bibbins-Domingo and Fernandez note, many academic medical centers have ventured into population health with its focus on prevention and broader issues affecting people’s health status, including upstream, social determinants. In some cases, those population health efforts and programs have led to formal and informal partnerships with community organizations and departments of health.

“These movements in academic medical centers are laudable and, based on our experience, argue for more formal training and recognition of the academic physicians who are leading and partnering with others to advance population health,” they argued.

Bibbins-Domingo and Fernandez point to the 1910 Flexner report as putting U.S. medical school on the path toward research excellence and “enshrinement of the biomedical model of clinical care.” Another Flexner-like overhaul of American medical schools is not in the offing, but they say in light of the 21st century healthcare challenges — they mention obesity, the opioid epidemic and infectious diseases — it is time to invest in another kind of academic clinical leader.

—Peter Wehrwein

Listen to our podcasts!

MRI has become part of everyday healthcare. But for many people in the U.S., access to MRI imaging services is problematic. In rural areas, people may need to travel long distances. The design of the machines may be a barrier.

Managed Healthcare Executive* (MHE) Editor Briana Contreras heard MRI access issues firsthand recently from Wes Gilson, a senior director at Siemens Healthineers, a German healthcare technology company that manufacturers MRI scanners. Gilson discussed how improving access to MRI services can improve healthcare equity and also innovations in MRI technology and their relationship to access.

“MHE Talks: Improving Patient Access” is a subseries focused of MHE’s main podcast “Tuning In to the C-Suite,” which spotlights healthcare professionals, leaders and executives talking with the editors crucial issues in American healthcare.

Have a suggestion for a future guest? Please drop Briana Contreras a line at BContreras@mjhlifesciences.com.

Also featured on the podcast is another subseries, “Meet the Board,” which spotlights members of the MHE editorial advisory board.

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Multiple sclerosis
Some drugs new, some tried-and-true

Multiple sclerosis (MS) is a progressive autoimmune disease that affects nearly 1 million people in the United States. The debilitating disorder is characterized by lesion formation throughout the central nervous system (CNS), brought on by demyelination and inflammation of different components of the CNS. Wayward B cells, T cells, monocytes, macrophages and microglia are responsible for wreaking this havoc. Several up-and-coming treatments home in on these cells with increasing specificity.

The disease has been grouped into four types that are based on the overall course of the disease and frequency of symptoms. Relapsing-remitting MS (RRMS) is the most common type, accounting for approximately 85% of cases. It is characterized as episodes of new or worsening symptoms (relapse), followed by recovery periods (remitance). Over time, RRMS typically changes into secondary-progressive MS (SPMS). Someone with SPMS experiences steadily worsening MS-associated symptoms and disability. Roughly 15% to 20% of people with MS have the primary-progressive (PPMS) form of the disease in which they experience gradual disease progression from the start without the relapse-recovery cycle of RRMS. Progressive-relapsing MS (PRMS) is the least common form of the disorder. People with PRMS experience gradual deterioration from the start but may also have relapsing periods similar to those seen in patients with RRMS.

Given that RRMS is, by far, the most common type of MS, it is not surprising that currently available drugs primarily target this form of the disease. However, some new agents in development may change that. These drugs include a new class for MS treatment and potential therapies for progressive forms of MS.

Bruton tyrosine kinase inhibitors

Three potential newcomers to the MS armamentarium are racing through the pipeline as they compete to be the first-in-class Bruton tyrosine kinase (BTK) inhibitor. BTK is a nonreceptor kinase that plays a critical role in signal transmission through B cells and myeloid cells, both of which are significantly involved in MS pathology. Drugs that inhibit BTK can block the activation of B cells, thereby inhibiting the release of proinflammatory cytokines that are responsible for MS symptoms and disease progression.

Evobrutinib, developed by Merck, is an oral selective and irreversible BTK inhibitor that interferes with B-cell activation and macrophage activity. It also hinders B cells from acting as antigen-presenting cells, thereby reducing inflammation in the CNS. In phase 2 trials, evobrutinib significantly reduced the number of active lesions in participants with RRMS but had no effect on relapse rate or progression of disability. The drug is currently under investigation in phase 3 trials as a treatment for RRMS.

Competing with evobrutinib is Sanofi’s tolebrutinib, which is another BTK inhibitor that is under investigation for the treatment of relapsing forms of MS. In a phase 2 trial, tolebrutinib achieved primary and secondary end points, with at least 85% relative reduction in new or enlarging lesions. Because of this drug’s mechanism, it affects B cells and CNS microglial cells, both of which are thought to be involved in neuroinflammation and neurodegeneration. Because it can cross the blood-brain barrier, tolebrutinib may have additional capabilities.
that the company intends to research further. The drug is currently in phase 3 trials, evaluating its efficacy in the treatment of RRMS and disability progression. Roche’s fenebrutinib may potentially address the scarcity of treatments for the progressive forms of MS. The company believes the drug may offer a new mechanism to suppress MS activity and slow disease progression through its ability to inhibit the activation of both B cells and myeloid lineage cells. Additionally, fenebrutinib may be associated with fewer side effects than evobrutinib and tolebrutinib. The drug is currently in phase 3 trials as a treatment for RRMS, PRMS and PPMS.

Masitinib
Masitinib, developed by AB Science, a French biotech company, is an oral tyrosine kinase inhibitor that targets mast cells and microglia. Similar to fenebrutinib, masitinib has been developed to treat the progressive forms of MS. Findings from phase 2b/3 trials indicate masitinib can significantly slow disease progression in adults with PPMS and nonactive SPMS. Another phase 3 trial has been planned to confirm these results in a larger population.

Ublituximab
Ublituximab is a potent glycoengineered anti-CD20 monoclonal antibody that is currently in phase 3 studies for the treatment of RRMS. Ublituximab targets an epitope on B cells that express CD20. By binding to B cells, ublituximab triggers both antibody-dependent cellular cytotoxicity and complement-dependent cellular cytotoxicity, leading to cell death. The hope is that by eradicating B cells responsible for much of MS pathology, ublituximab can slow disease progression and reduce or prevent further damage in the CNS.

TG Therapeutics, a North Carolina biotech company, has submitted an application to the FDA for the approval of ublituximab, and the agency is expected to make a decision in September 2022. If approved, ublituximab would join Roche’s Ocrevus (ocrelizumab) and Novartis’ Kesimpta (ofatumumab) as the third anti-CD20 monoclonal antibody approved by the FDA as a treatment for relapsing MS. One of ublituximab’s possible advantages is that it takes less time to infuse.

Vidofludimus calcium
Vidofludimus calcium, developed by Immunic Therapeutics, a New York biotech company, is designed to repress proinflammatory cytokines produced by T helper cells, thereby reducing inflammation associated with MS. The manufacturer sees several advantages to this drug over existing therapies, including a favorable side effect profile. Vidofludimus calcium is currently in phase 3 trials for potential use in RRMS.

Old drugs, new tricks
Drug repurposing is catching the eye of drug developers, partly because using known entities can shorten the time it takes to put a drug through trials and gain FDA approval. Three established drugs are under investigation as potential MS treatments.

Statins, approved as agents that lower low-density lipoprotein cholesterol levels, are also known to have anti-inflammatory and neuroprotective properties. Simvastatin is being investigated as a potential treatment of PPMS and SPMS. A phase 2 study demonstrated that high doses of simvastatin reduced brain atrophy by 43% compared with placebo, and it slowed the progression of physical disability and cognitive decline in individuals with SPMS. After these encouraging results, Jeremy Chataway of University College London Institute of Neurology, and his colleagues launched a phase 3 trial evaluating the efficacy of simvastatin in slowing disease progression in patients with SPMS.

Metformin has been used in the United States for nearly three decades to lower glucose production and enhance insulin sensitivity in people with Type 2 diabetes. The Multiple Sclerosis Society UK in London is sponsoring a phase 2 trial to evaluate whether metformin combined with clemastine, an antihistamine, can stimulate the brain to generate new myelin.

Clemastine is thought to signal stem cells to begin myelin repair, whereas metformin puts the cells in a position to respond to the signal. If the metformin-clemastine combination proves to be safe and effective, it would become the first treatment to promote neuron remyelination in patients with MS.
For patients with Homozygous FH (HoFH) aged 12 years or older¹

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*The LDL-C—lowering effect of EVKEEZA may be measured as early as 2 weeks. At week 24, the LS mean treatment difference between EVKEEZA and placebo in mean percent change in LDL-C from baseline was -49% (95% CI: -65% to -33%, <0.0001).

**INDICATION**
EVKEEZA® is an ANGPTL3 (angiopoietin-like 3) inhibitor indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).

**Limitations of Use:**
- The safety and effectiveness of EVKEEZA have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HeFH).
- The effects of EVKEEZA on cardiovascular morbidity and mortality have not been determined.

**IMPORTANT SAFETY INFORMATION**

**Contraindication**
EVKEEZA is contraindicated in patients with a history of serious hypersensitivity reactions to evinacumab-dgrb or to any of the excipients in EVKEEZA. Serious hypersensitivity reactions, including anaphylaxis, have occurred.

**Warnings and Precautions**

**Serious Hypersensitivity Reactions:** Serious hypersensitivity reactions have occurred with EVKEEZA. If signs or symptoms of serious allergic reactions occur, discontinue EVKEEZA infusion, treat according to the standard-of-care, and monitor until signs and symptoms resolve.

Visit **EVKEEZAhcp.com** to learn more about EVKEEZA
EVKEEZA® lowered LDL-C by ~50%, on average, at 24 weeks¹

Study design
The efficacy and safety of EVKEEZA in the treatment of HoFH was demonstrated in a multicenter, double-blind, randomized, placebo-controlled study in patients with HoFH. The mean age of patients at baseline was 42 years (range: 12 to 75 years). Patients were on a background of LLTs, including maximally tolerated statins, ezetimibe, PCSK9 inhibitor antibodies, lomitapide, and lipoprotein apheresis. The mean LDL-C at baseline was 255 mg/dL. In the double-blind treatment period, 43 patients were randomized to receive EVKEEZA 15 mg/kg IV every 4 weeks and 22 patients to receive placebo. In the open-label treatment period, 64 patients received EVKEEZA 15 mg/kg IV every 4 weeks.¹

The primary endpoint was percent change in LDL-C from baseline to week 24. At week 24, the LS mean treatment difference between EVKEEZA and placebo was -47% (95% CI: -65% to -39%; P <0.001) and -52% (95% CI: -65% to -39%; P <0.001).¹

A key secondary endpoint was the LS mean change in LDL-C from baseline to week 24. At week 24, the LS mean change in LDL-C from baseline for patients receiving EVKEEZA was -135 mg/dL compared with -3 mg/dL for patients receiving placebo (treatment difference -132 mg/dL; 95% CI: -175 to -89; P <0.001).²

At week 24, the LS mean difference between EVKEEZA and placebo for ApoB and non-HDL-C was -37% (95% CI: -49% to -25%; P <0.001) and -52% (95% CI: -65% to -39%; P <0.001), respectively.²

Apob=apolipoprotein B; CI=confidence interval; DBTP=double-blind treatment period; IV=intravenous; non-HDL-C=non-high-density lipoprotein-cholesterol; PCSK9=proprotein convertase subtilisin kexin type 9; SE=standard error.

IMPORTANT SAFETY INFORMATION (continued)
Embryo-Fetal Toxicity: EVKEEZA may cause fetal harm when administered to pregnant patients. Advise patients who may become pregnant of the risk to a fetus. Consider obtaining a pregnancy test prior to initiating treatment with EVKEEZA. Advise patients who may become pregnant to use effective contraception during treatment and for at least 5 months following the last dose.

Adverse Reactions
Common adverse reactions (≥5%) were nasopharyngitis (16%), influenza-like illness (7%), dizziness (6%), rhinorrhea (5%), and nausea (5%).

Use in Specific Populations
Pregnancy: EVKEEZA may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. If a patient becomes pregnant while receiving EVKEEZA, healthcare providers should report EVKEEZA exposure by calling 1-833-385-3392.

Lactation: There are no data on the presence of evinacumab-dgnb in human milk or animal milk, the effects on the breastfed infant, or the effects on milk production. Maternal IgG is known to be present in human milk. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for EVKEEZA and any potential adverse effects on the breastfed infant from EVKEEZA or from the underlying maternal condition.

Females and Males of Reproductive Potential: Consider pregnancy testing in patients who may become pregnant prior to starting treatment with EVKEEZA. EVKEEZA may cause fetal harm when administered to a pregnant woman. Females of reproductive potential should use effective contraception during treatment with EVKEEZA and for at least 5 months following the last dose of EVKEEZA.

Pediatrics: The safety and efficacy of EVKEEZA have not been established in pediatric patients with HoFH who are younger than 12 years old.

Please see Brief Summary of full Prescribing Information on the next page.

EVKEEZA (evinacumab-dgnb) injection, for intravenous use

Brief Summary of Prescribing Information

1  INDICATIONS AND USAGE

EVKEEZA is an ANGPTL3 (angiopeptin-like 3) inhibitor indicated as an adjunct to other low-density lipoprotein-cholesterol (LDL-C) lowering therapies for the treatment of adult and pediatric patients, aged 12 years and older, with homozygous familial hypercholesterolemia (HoFH).

Limitations of Use:

- The safety and effectiveness of EVKEEZA have not been established in patients with other causes of hypercholesterolemia, including those with heterozygous familial hypercholesterolemia (HoFH).
- The effects of EVKEEZA on cardiovascular morbidity and mortality have not been determined.

4  CONTRAINDICATIONS

EVKEEZA is contraindicated in patients with a history of serious hypersensitivity reaction to evinacumab-dgnb [see Contraindications (4)].

5  WARNINGS AND PRECAUTIONS

5.1 Serious Hypersensitivity Reactions

Serious hypersensitivity reactions have occurred with EVKEEZA. In clinical trials, 1 (1%) EVKEEZA-treated patient experienced anaphylaxis versus 0 (0%) patients who received placebo. If signs or symptoms of serious hypersensitivity reactions occur, discontinue EVKEEZA infusion, treat according to the standard-of-care, and monitor until signs and symptoms resolve. EVKEEZA is contraindicated in patients with a history of serious hypersensitivity reaction to evinacumab-dgnb [see Contraindications (4)].

5.2 Embryo-Fetal Toxicity

Based on the findings in animal reproduction studies, EVKEEZA may cause fetal harm when administered to pregnant rabbits during organogenesis caused increases in fetal malformations at doses below the human exposure. Advise patients who may become pregnant of the risk to a fetus. Consider obtaining a pregnancy test prior to initiating treatment with EVKEEZA. Adverse patients who may become pregnant to use effective contraception during treatment with EVKEEZA and for at least 5 months following the last dose of EVKEEZA [see Use in Specific Populations (5.4)].

6  ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity Reactions [see Warnings and Precautions (5.1)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adverse reactions reported in randomized, double-blind, placebo-controlled trials that included 100 patients treated with EVKEEZA. The mean age of EVKEEZA-treated patients was 50 years (range: 18 to 75 years). 52% were women, 5% were Hispanic, 8% were Black, 6% were Asian, 5% were White, 5% were Other, 4% were American Indian or Alaska Native, 4% were Asian, and 1% were Others. The most common adverse reactions reported in greater than 3% of EVKEEZA-treated patients and more frequently than in placebo are shown in Table 1.

Table 1: Adverse Reactions Occurring in ≥3% of Patients Treated with EVKEEZA and Greater than Placebo in 24-Week, Pooled, Placebo-Controlled Trials

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Placebo (n=54)</th>
<th>EVKEEZA (n=96)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasopharyngitis</td>
<td>13%</td>
<td>16%</td>
</tr>
<tr>
<td>Influenza-like illness</td>
<td>6%</td>
<td>7%</td>
</tr>
<tr>
<td>Gout</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>0%</td>
<td>5%</td>
</tr>
<tr>
<td>Nausea</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>0%</td>
<td>4%</td>
</tr>
<tr>
<td>Urticaaria</td>
<td>0%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Other adverse reactions occurring in less than 3% of patients treated with EVKEEZA and greater than placebo included constipation, upper respiratory tract infection, nasopharyngitis, and rhinitis.

Transient, mild to moderate decrease in diastolic blood pressure and increases in heart rate occurred in clinical trials of EVKEEZA infusion but did not require intervention and resolved post-infusion.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EVKEEZA in the studies described below with the incidence of antibodies in other studies or to other products may be misleading.

No patients developed treatment-emergent antibodies to EVKEEZA.

8  USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on data from animal reproduction studies, EVKEEZA may cause fetal harm when administered to pregnant patients. Available human data are insufficient to evaluate a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Evinacumab-dgnb is a human IgG monoclonal antibody [see Description (11) in the full prescribing information] and human IgG is known to cross the placental barrier; therefore, evinacumab-dgnb has the potential to be transmitted from the mother to the developing fetus.

Subcutaneous administration of evinacumab-dgnb to pregnant rabbits during the period of organogenesis resulted in fetal malformations (dowed head, exencephaly, and flexed limbs) at doses below the maximum recommended human dose (MRHD). No adverse embryofetal effects were observed with subcutaneous administration of evinacumab-dgnb to pregnant rats during the period of organogenesis at doses below the MRHD. Measurable evinacumab-dgnb serum concentrations were observed in fetal rabbit and rat sera at birth, indicating that evinacumab-dgnb, like other IgG antibodies, crosses the placental barrier [see Data]. Advise pregnant women of the potential risk to a fetus.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

If a patient becomes pregnant while receiving EVKEEZA, healthcare providers should report EVKEEZA exposure by calling 1-833-380-5392.

Data

Animal Data

In an embryo-fetal development study in pregnant rabbits, evinacumab-dgnb was administered subcutaneously at doses of 1, 5, 10 and 30 mg/kg every 3 days (Q3D) during the period of organogenesis from gestation day 7 to day 19. Evinacumab-dgnb was teratogenic in rabbits, causing dowed head, dilation of the lateral and third ventricles of the brain, and flexed fore/hind paws at maternal evinacumab-dgnb concentrations above human exposure at the MRHD of 15 mg/kg every 4 weeks, based on AUC. Other fetal malformations, consisting of irregular and abnormal ossification in the skull, palate, metacarpal, and enlarged anterior and/or posterior fontanelles occurred and were consistent with significant maternal toxicity (including early deaths due to abortion and premature delivery at all doses, reduction in maternal body weight gains, and reduction in maternal food consumption) in addition to increased post-implantation losses, resorptions (total, early, and late), and decreased fetal body weight were also consistent with maternal toxicity. Evinacumab-dgnb was present in the sera of fetuses born from mothers at 10 and 30 mg/kg/Q3D at levels higher than in maternal serum.

In an embryo-fetal development study in pregnant rats, evinacumab-dgnb was administered subcutaneously at doses of 5, 10, 30 and 100 mg/kg/Q3D during the period of organogenesis from gestation day 6 to day 18. Maternal exposures to evinacumab-dgnb were below the human exposure measured at the MRHD. Evinacumab-dgnb resulted in unexplained maternal deaths at 100 mg/kg/Q3D. Evinacumab-dgnb crossed the placenta and was present at ratios (C fetal/CMaternal) ranging from 0.42 to 0.58. No adverse effects on embryofetal development were observed at any dose.

In a combined fertility, embryofetal, and pre- and postnatal development study, female rats were administered evinacumab-dgnb via subcutaneous injection at doses of 30 and 100 mg/kg/Q3D beginning 2 weeks prior to mating and continuing to gestation day 21 or lactation day 21. Maternal systemic exposures were below the human exposure at the MRHD throughout the study. No maternal or developmental toxicity was observed.

8.2 Lactation

Risk Summary

There are no data on the presence of evinacumab-dgnb in human milk or animal milk, the effects on baby, the effects on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed infant to evinacumab-dgnb are unknown.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for EVKEEZA and any potential adverse effects on the breastfed infant or the nursing mother’s health.

8.3 Females and Males of Reproductive Potential

Pregnancy Testing

Consider pregnancy testing in patients who may become pregnant prior to starting treatment with EVKEEZA [see Warnings and Precautions (5.2) and Use in Specific Populations (8.1)]

Contraception

Females

Based on animal studies, EVKEEZA may cause fetal harm when administered to pregnant patients [see Use in Specific Populations (8.1)]. Patients who may become pregnant should use effective contraception during treatment with EVKEEZA and for at least 5 months following the last dose of EVKEEZA.

8.4 Pediatric Use

The safety and effectiveness of EVKEEZA as an adjunct to other LDL-C-lowering therapies for the treatment of HoFH have been established in pediatric patients aged 12 years and older. Use of EVKEEZA for this indication is supported by evidence from adequate and well-controlled trials in adults with additional efficacy and safety data in pediatric patients aged 12 years and older [see Adverse Reactions (6.1) and Clinical Studies (16)].

The safety and effectiveness of EVKEEZA have not been established in pediatric patients with HoFH who are younger than 12 years old.

8.5 Geriatric Use

Clinical studies of EVKEEZA did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

REGENERON

Manufactured by:

Regeneron Pharmaceuticals, Inc.

777 Old Saw Mill River Road

Tarrytown, NY 10591-6707

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03/2021

Regeneron Pharmaceuticals, Inc.

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AI for fraud detection

Humans still have a role, but in a recent survey, about half of insurers said they are using AI to help cut down on fraud, waste and abuse. 

The era of big data has led to a transformation of healthcare, including the ability for providers to leverage massive amounts of real-world data to help inform high-stakes clinical decisions. Yet, when it comes to fraud, waste and abuse (FWA), big data can also make it easier to bury the needles of fraudulent claims in an ever-growing haystack of data.

But maybe the “needle” metaphor does not do justice to the scale of FWA. The National Health Care Anti-Fraud Association said a conservative estimate is that approximately 3% of annual healthcare spending is spent on fraudulent claims, whereas other estimates put that number closer to 10% of total healthcare spending, which would translate to over $300 billion annually. In fact, just a single company, Highmark Inc., reported savings of $245 million as a result of efforts to combat FWA. The Pittsburgh-based insurer said its savings were due to the work of the company’s Financial Investigations and Provider Review department, but they were also thanks to the department’s artificial intelligence (AI) software.

“AI allows Highmark to detect and prevent suspicious activity more quickly, update insurance policies and guidelines, and stay ahead of new schemes and bad actors,” says Melissa Anderson, Highmark’s chief auditor and compliance officer.

Highmark is not alone. A host of software providers are now offering AI products designed to identify errors or unusual activity that may be indicative of fraud. A report released in July 2021 by PYMNTS.com and Brighterion AI, a Mastercard company, found 44% of the largest insurers it surveyed were using AI to detect FWA. The report was based on a survey of 100 healthcare executives with responsibilities for or direct knowledge of FWA.

Jodi G. Daniel, a partner at Crowell & Moring LLP, says AI can be a powerful tool in a data-heavy industry like healthcare. “When you’re talking about massive amounts of data, technology can help to detect patterns and can flag things that may be out of the ordinary or suspicious, so a human being can look at it,” she notes. Daniel leads the law firm’s digital health practice and previously headed the Office of Policy in the Office of the National Coordinator for Health Information Technology.

Worry about false positives

Health insurers are also proceeding with some caution. The insurance executives indicated in the Brighterion AI survey that cost savings, regulatory pressures and a high level of adaptability were important factors when choosing an AI provider, but they also cited accuracy as a key concern (95%). That’s because false positives — cases that look like fraud at first glance but are legitimate — are a major hurdle in terms of managing FWA, the report found.

In fact, among the largest companies surveyed, 66% said reducing false positives was “extremely important” when choosing an AI provider. Increasing detection of FWA with AI was labeled extremely important by only 25% of executives from the largest insurers. Among smaller insurers, reducing false positives was less likely to be extremely important (30%), and increasing FWA detection was more likely to be labeled extremely important (53%).

Daniel says that accuracy is important with any AI tool, which is why regulators prefer to see a human involvement not just software. She also says there is great risk associated with full automation, particularly in cases involving treatment decisions. “If you look at (FDA) oversight of clinical decision support tools, they treat tools that have a physician intermediary or clinician intermediary very differently than those that are fully automated,” says Daniel.

Jared Kaltwasser is a freelance writer in Iowa and a regular contributor to Managed Healthcare Executive®

Managed Healthcare Executive.com
IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.
- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

This material is intended for use by payers, formulary committees, or other similar entities for purposes of population-based drug selection, coverage, and/or reimbursement decision making, pursuant to FD&C Act Section 502(a).

EYLEA is a registered trademark of Regeneron Pharmaceuticals, Inc.
• **Powerful efficacy** and **robust anatomic outcomes** across all indications as shown in 8 phase 3 clinical trials¹-⁸
  • A broad range of indications and **dosing flexibility** across several FDA-approved indications²

• **Demonstrated safety** profile across 4 VEGF-driven retinal diseases: Wet AMD, DR, DME, and MEIRVO¹
  • As of March 31, 2020, postmarketing reports in the global safety database of IOI or retinal vasculitis have accounted for **1 out of every 6 million injections** (0.00002%), and all such cases were associated with endophthalmitis

• **10 years** of extensive real-world experience¹ and >20 million doses administered to >1.6 million eyes since launch (and counting)³
  • Established and consistent **dosing options**
  • **Stable pricing** since launch in 2011

DME = diabetic macular edema; DR = diabetic retinopathy; FDA = US Food and Drug Administration; IOI = intraocular occlusion; MEIRVO = macular edema following retinal vein occlusion; RAO = retinal arterial occlusion; VEGF = vascular endothelial growth factor.

**ADVERSE REACTIONS**

• Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
  • The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.
  • Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

**INDICATIONS**

EYLEA® (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

References:

Please see Brief Summary of full Prescribing Information on the following page.


**Table 1: Most Common Adverse Reactions (≥1%) in Wet AMD Studies**

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Baseline to Week 52</th>
<th>Baseline to Week 96</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EYLEA (N=142)</strong></td>
<td><strong>Control (N=147)</strong></td>
<td><strong>EYLEA (N=287)</strong></td>
</tr>
<tr>
<td>Eye pain</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Conjunctival hyperemia</td>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Macular edema</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>Foreign body sensation in eyes</td>
<td>3%</td>
<td>3%</td>
</tr>
</tbody>
</table>

For more information, see the EYLEA full Prescribing Information available on HOPEYELAUS for additional product information.
Mark Cuban says he has the prescription for high, opaque drug pricing

Cuban, an investor on “Shark Tank” and owner of the NBA’s Dallas Mavericks, has launched a namesake online pharmacy that says it will have transparent pricing and will bypass pharmacy benefit managers. by SUSAN LADIKA

A new online pharmacy founded by Mark Cuban, billionaire investor and Dallas Mavericks owner, hopes to be a slam dunk when it comes to drawing in consumers who are seeking an alternative to paying high prices for essential drugs. The Mark Cuban Cost Plus Drug Company launched in January and offers what it claims are the lowest prices available on 100 generic drugs.

With this online pharmacy, “consumers can get access to routine drugs at lower costs, forcing other organizations in the industry to meet or beat it,” says Amel Hammad, managing director and leader of the healthcare industry practice of Riveron Consulting.

A major part of Cuban’s pharmacy pitch is that it will be transparent about pricing. The new pharmacy says it sets prices based on the cost to manufacture the drug, plus a 15% markup for each drug it dispenses, and a $3 charge for labor. The consumer pays for shipping. In the press release announcing the venture, Cuban’s online pharmacy held up Gleevec (imatinib), a cancer drug, as an example, stating that Gleevec retails for $9,657 per month, but the generic version can be purchased through the new online pharmacy for just $47.

Cuban’s online pharmacy is also promising good deals on less expensive drugs. The company’s website is pricing a 30-day supply of lisinopril, a blood pressure medication, at $3.60. The company says, by contrast, a 30-day supply sells for $24 at retail pharmacies. However, that is a bit misleading, because GoodRx lists prices that are less than half that at several retail pharmacies with a price of $4 for a 30-day supply.

Cuban’s new company doesn’t accept insurance payment, so anyone buying drugs from the online pharmacy will be paying out of pocket. But “often, the same drug is cheaper than it is with an insurance copay,” says Lovisa Gustafsson, MBA, vice president at the Commonwealth Fund, a foundation that focuses on healthcare research.

Hunger for lower prices
Cuban is starting his pharmacy when there is widespread discontent with the drug costs. President Joseph R. Biden mentioned high drug prices in his State of the Union address in February. According to the federal government actuaries, expenditures on prescription drugs topped $348 billion in 2020, which is up 3% from the previous year. A study released this past year by RAND Corporation found that prescription drug prices in the United States were, on average, 2.56 times higher than in the 32 other countries in the study. For brand-name drugs, U.S. prices averaged 3.44 times higher. However, generic drug prices in the U.S. were slightly lower. Generic drugs account for almost 85% of drugs that are sold in the U.S. but just 12% of spending, RAND found.

Poll results released in September by Gallup showed that 18 million Americans couldn’t afford at least one of their medications in the previous three months. The problem of affordability was especially serious for those earning less than $24,000 per year. However, the pricing of drugs in the U.S. is complicated by a web of rebates and discounts that separate the stated price from the one actually paid. By some accounts, trends in net prices paid by insurers and other payers have been flat and have even dipped in recent years.

Cuban’s online pharmacy may be particularly attractive for those who pay out of pocket for their prescriptions, which is a group that would include people without insurance or those who have signed up for a high deductible plan, says Stacie Dusetzina, Ph.D., associate professor of health policy at Vanderbilt University. However, “the challenge is that...
they are somewhat limited in scope,” Dusetzina says, noting that Cuban’s pharmacy is offering only a limited selection of generic drugs. In addition, Hammad says the new online pharmacy may help address access because of the mail-order delivery, although mail-order delivery is hardly unique to Cuban’s new pharmacy.

**Cutting out the “bouncers”**

The inspiration for Cuban’s pharmacy came from an email Alex Oshmyansky, M.D., Ph.D., sent to Cuban, who is perhaps best known for being one of the investors on the television show, “Shark Tank.” Oshmyansky, a radiologist who earned his medical degree from Duke University and trained at Harvard University and Johns Hopkins, was seeking investment in his company, Osh’s Affordable Pharmaceuticals, according to Texas Monthly. Oshmyansky had set up the company to purchase generic drugs directly from manufacturers and sell them to pharmacies, thereby cutting out the pharmacy benefit managers (PBMs).

In an interview with NPR, Cuban said he asked Oshmyansky, who now serves as CEO of Cuban’s online pharmacy, “Can we cut out the inefficiencies?” Cuban’s company has created its own PBM to work with the manufacturers, and later this year, the company is set to open a manufacturing facility in Dallas.

On NPR, Cuban likened PBMs to “bouncers at a club,” saying they are “controlling access to all the big insurers. And if you want this insurance company to sell your drug, you’ve got to pay the cover charge,” which comes in the form of rebates paid by drugmakers. When the Wall Street Journal reported on Cuban’s new enterprise in October 2021, months before the official announcement, the newspaper characterized the venture as a PBM.

Cuban’s operation has “found a way to address pain points around prescription drugs by going directly to the manufacturers to avoid the markup created by the healthcare industry while cutting out the middlemen of third-party insurance and pharmacies,” Hammad says.

Ventures such as Cuban’s are a “pushback against middlemen,” Gustafsson says. “(It will be) interesting to see how successful they are,” Gustafsson says, especially as they scale up their offerings over time.

Because the new pharmacy doesn’t take insurance and only offers a subset of generic drugs, Dusetzina says she’s unsure of how disruptive this would be to a PBM.

**Other disrupters**

Cuban’s venture is “one in a broader trend of new entrants to the pharmaceutical supply chain,” Gustafsson says. Amazon also has an online pharmacy, she notes. Prices are posted on the website and payments from most major insurers are accepted. In addition, Amazon Prime members get extra savings.

Gustafsson says the new entrants in the drug supply chain could eventually have an impact on PBMs if the companies wind up negotiating on behalf of fewer people.

“Innovators in healthcare understand the pain points consumers are encountering,” Hammad says. “They recognize many people are willing to take the private-pay approach, and not utilize insurance or any third-party payer, to avoid the administrative burden.”

Susan Ladika is an independent journalist in Tampa, Florida, who covers business and healthcare.
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The thinking was that infectious diseases were behind us, a problem of the past and of impoverished places that were stuck in the past. Antibiotics, better sanitation, improved nutrition, a higher standard of living—they combined to push infectious diseases to the margins of health concerns. Twentieth century public health experts called it the epidemiologic transition, from a healthcare past dominated by diseases, such as tuberculosis, diphtheria and typhoid fever, to a healthcare present and future concerned with heart disease, cancer and diabetes.

“The most remarkable change in patterns of health during the (past) century has been the largely successful conquest of infectious diseases,” wrote Allan Brandt, Harvard medical historian, in “No Magic Bullet: A Social History of Venereal Disease in the United States Since 1880,” his highly regarded history of venereal disease that was first published in 1985.

When Ezekiel Emanuel, M.D., Ph.D., an oncologist and prominent health policy expert at the
COVID-19 breaks into the top 10

COVID-19 was nowhere to be seen in 2019 as a cause of death. In 2020, it became the third leading cause of death in the U.S., surpassing unintentional injuries (drug overdoses, motor vehicle accidents, falls), stroke and chronic lower respiratory diseases.

Age-adjusted death rates for the 10 leading causes of death in the United States, 2019 and 2020

In March in the *Lancet*. Their figures show 824,000 reported COVID-19 deaths in the U.S. from Jan. 1, 2020, to Dec. 31, 2021. They also tabulated excess mortality. Worldwide, it was over three times greater than the number of reported COVID-19 deaths (18.2 million compared with 5.9 million). For the U.S., the researchers put the excess mortality at 1.13 million. Reasons for the difference between excess mortality and reported COVID-19 deaths include the possibility of undercounting COVID-19 deaths and knock-on effects of the pandemic, such as deaths from delays in healthcare or the widely documented worsening of mental health.

COVID-19 made it impossible to ignore the enormous disruptive power of an infectious disease. However, there were plenty of warnings before 2020. In 1992, the Institute of Medicine (now called the National Academy of Medicine) released “Emerging Infections: Microbial Threats to Health in the United States.” Two years later, journalist Laurie Garrett sounded the alarm with her book, “The Coming Plague: Newly Emerging Diseases in a World Out of Balance.” And the plagues — although not as infectious and lethal — did come. Novel diseases
Infectious Diseases  |  Finding a way forward for public health

Top 10 causes of death and disability (DALYs) in 2019 and percent change from 2009-2019

<table>
<thead>
<tr>
<th>No.</th>
<th>Condition</th>
<th>Noncommunicable diseases</th>
<th>Injuries</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Ischemic heart disease</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>2.</td>
<td>Drug use disorders</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>3.</td>
<td>Low back pain</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>4.</td>
<td>COPD</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>5.</td>
<td>Diabetes</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>6.</td>
<td>Lung cancer</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>7.</td>
<td>Stroke</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>8.</td>
<td>Other musculoskeletal</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>9.</td>
<td>Depressive disorders</td>
<td>20%</td>
<td>80%</td>
</tr>
<tr>
<td>10.</td>
<td>Road injuries</td>
<td>20%</td>
<td>80%</td>
</tr>
</tbody>
</table>

DALY = disability-adjusted life years. COPD = chronic obstructive pulmonary disease

have punctuated the past two decades, including the West Nile virus (1999); severe acute respiratory syndrome (2003), which, like COVID-19, is caused by a coronavirus; H1N1 influenza (2009); Ebola (2014); and Zika (2009).

Ira Wilson, M.D., Sc.M., a professor and chair of the Department of Health Services, Policy and Practice at the Brown University School of Public Health in Providence, Rhode Island, notes there was a transition away from infectious diseases in the 20th century, but many of those diseases were bacterial and therefore were treatable with antibiotics. These novel 21st-century infectious diseases are viral and harbored by animals. Experts in these zoonotic diseases point to deforestation and other factors as bringing human beings into closer contact with many animals, Wilson explained. “The first transition had to do (with mostly) poverty and bacterial diseases, so people were less likely to die of infections. They died of other things,” he says. “This is a different or new transition. Humans are invading ecosystems that have evolved without them.”

CHUTES AND LADDERS
The epidemiological transition envisioned decades that often depicted the post-infectious disease problems of heart disease and cancers as “diseases of affluence.” That is another concept that is out of step with these times, notes Theo Vos, M.D., Ph.D., M.Sc., professor of health metrics sciences at the Institute for Health Metrics and Evaluation and a member of the senior management team. “Diseases of affluence are diseases of poverty in the U.S.,” Vos says, “That was maybe coined 30 (or) 40 years ago. There are (more) rates of obesity, diabetes, heart disease and quite a few cancers among poorer people.”

So rather than a smooth glide path from infectious disease to so-called diseases of affluence, the 21st-century epidemiologic transition seems more like a game of chutes and ladders: progress here, regress there. How might the U.S. healthcare system respond and adjust to this era of viral disease outbreaks and uneven distribution of disease? There’s no end to the answers to those questions. And the questions have been posed in many different ways.

For decades, both providers and payers in the U.S. have been oriented toward dealing with acute episodes of disease and injuries, with perhaps some attention to a few chronic conditions. Public health, with its orientation toward prevention, has been way down on almost any list of healthcare priorities. Spending on public health shot up in 2020 because of the pandemic, but in 2019, it totaled $105 billion, according to the annual report on U.S. health expenditures that the CMS Office of the Actuary issued earlier this year. That is less than 3% of the $3.75 trillion the U.S. spent on healthcare that year and approximately 9% of the $1.19 trillion the country spent on hospital care.

Rodrigo Cerdá, M.D., M.P.H. medical director of Independence Blue Cross in Philadelphia and member of the Managed Healthcare Executive®
Finding a way forward for public health

Infectious Diseases

Excess mortality far outpaces COVID-19 deaths

Between Jan. 1, 2020, and Dec. 31, 2021, the excess mortality worldwide was three times larger than the reported number of COVID-19 deaths (18.2 million vs. 5.94 million) and in the U.S., the excess mortality exceeded the reported number of COVID-19 deaths by 37% (1.13 million vs. 824,000).

<table>
<thead>
<tr>
<th></th>
<th>Reported COVID-19 deaths</th>
<th>Reported COVID-19 mortality rate (per 100,000)</th>
<th>Excess mortality</th>
<th>Excess mortality rate (per 100,000)</th>
<th>Ratio of excess mortality to reported COVID-19 mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global*</td>
<td>5.94 million</td>
<td>39.2</td>
<td>18.2 million</td>
<td>120.3</td>
<td>3.07</td>
</tr>
<tr>
<td>U.S.</td>
<td>824,000</td>
<td>130.6</td>
<td>1.13 million</td>
<td>179.3</td>
<td>1.37</td>
</tr>
</tbody>
</table>

*Statistical model includes 191 countries based on 74 countries that reported data.

Source: Institute for Health Metrics and Evaluation, Lancet, March 2022

editorial advisory board, says U.S. healthcare is skewed toward rescue care. “We pay people a lot of money to get Johnnny out of the well over and over again, but we do not invest any money in building a little wall around the well so Johnnny doesn’t fall in,” Cerdá says.

The scanty funding for public health came up during a panel discussion about COVID-19 in February, which was jointly sponsored by STAT and ProPublica. “There have been a lot of finger points that have gone toward the sector of public health,” said Umair Shah, M.D., M.P.H., secretary of health for Washington State. “Why couldn’t you have done this faster? Why weren’t those systems available? Why wasn’t the staffing to those levels? Why didn’t you have the right technologies?” That all goes to this value system, where we have continued to value healthcare to the detriment of investment in public health.

Emanuel describes the U.S. healthcare system as being “neither fish nor fowl,” but like Cerdá, he references money spent on acute care and, more specifically, that approximately one-third of healthcare spending is on hospital care. However, Emanuel also notes the pandemic-fueled uptake of telehealth and remote care and how that trend may push more money into managing chronic disease and improve outcomes as a result.

BURDEN-OF-DISEASE CALCULATIONS

The Institute for Health Metrics and Evaluation was in the spotlight in 2020 during the early months of pandemic, when disease models projecting the number of deaths from COVID-19 flared up as hot news. However, the institute is known in health research and policy circles for its ambitious efforts to quantify the burden — how much early mortality and disability they cause — of disease and injuries. Thousands of researchers are involved in creating its Global Burden of Diseases, Injuries, and Risk Factors (GBD) study, which quantifies those burdens on a country-by-country basis. The Bill & Melinda Gates Foundation funds the effort. Ideally, governments and international organizations use the GBD research to match healthcare resources to healthcare needs.

Vos says the institute’s researchers are working on finalizing the COVID-19 burden-of-disease numbers. As the third leading cause of death in the U.S., it won’t be small, although the fact that COVID-19 disproportionately affects older people is something of an offsetting factor. Vos says long COVID-19 may come in at about 30th in the ranking of disabling conditions, “so not way up there but not trivial.” He doesn’t believe, though, the disease burden of COVID-19 and other recent disease outbreaks is so large as to merit a complete overhaul of U.S. healthcare system. “There are important things that have come out of this that we should learn from,” he says. “But there are still lots of people who will have problems with their eyes, have pain in their knees and so on. That’s not going to go away.”

Even so, there’s nothing like a public health crisis to stoke the appetite for more spending on public health. Federal spending on public health skyrocketed from $13.3 billion in 2019 to $128.2 billion in 2020, according to the CMS Office of the Actuary. The initial version of the now-stalled Build Back Better Act included $51 billion for public health infrastructure and pandemic preparedness. A year later, a scaled-back version of the legislation had $19.2 billion. The omnibus spending legislation
Finding a way forward for public health

Infectious Diseases

that funds the federal government through Sept. 30, 2022, includes a $582 million increase in funding for the CDC that is supposed to go toward public health infrastructure. Funding for global health programs increased by $634 million from the amounts allocated in 2021.

There are some differences of opinion about what public health infrastructure should entail, but improved surveillance and data collection and analysis seem to be on every list. “We need to invest a lot more in surveillance of potential candidates for yet another pandemic,” Vos says. “There are tools for that, and they are not dramatically expensive.” Furthermore, Emanuel was a co-author of a JAMA opinion piece that, among other things, called for creation of a “digital, real-time integrated data infrastructure for public health” as part of national strategy for dealing with COVID-19. Marc Lipsitch, D.Phil., an epidemiologist at the Harvard T.H. Chan School of Public Health in Boston, who was on the STAT-ProPublica panel with Shah, mentioned that he was “on loan” to the CDC this year to set up a center for forecast and outbreak analysis.

Other proposals for updating public health include building in reverse capacity, so when pandemics hit, hospital beds are ready and vaccines can be produced quickly. In the same JAMA opinion piece, Emanuel and his co-authors propose the creation of a public health workforce that could be dispatched to deal with emergencies and community health workers that could provide services outside of normal conventional healthcare settings.

Cerdá is concerned that when the COVID-19 pandemic fades, memory and preparedness will follow, so when the next pandemic occurs, the world will again be taken by surprise. He likens the need for investment in public health to the Federal Reserve and other institutions and policies designed to tamp down the economy’s boom-and-bust cycle.

“Maybe that is what we should be thinking about with public health — that this (pandemic) isn’t an exception (and) it is not different. We (must) have an infrastructure to address this, and it (must) be global,” Cerdá says.

However, Wilson says most public health systems don’t currently operate at the global scale. He sees a mismatch that is partly reflective of how the focus of public health tends to be at state and local levels.

Until 2020, when the pandemic forced the federal government to swing into action, combined state and local government spending on public health exceeded the federal government’s public health expenditures. “Public health is usually associated with units that are the size of countries or even states and counties. But COVID-19 is global and rips across all those borders and couldn’t care less about who is from where,” Wilson says. “Our political systems are ill-designed for the global problems we’ve created.”

For example, say there is enough money and that this sturdier and smarter public health infrastructure came to be — and it was accompanied by the thorough data collection and dazzling analytics — would that be enough to cope with future pandemics and viral disease outbreaks? Well, maybe.

But Cerdá, Wilson and others say the loss of trust in government and science will have a corrosive effect on even the most robust public health systems and measures. “There was an almost unquestioned trust of the CDC before the events of 2020. The loss of that trust is a very important loss,” says Cerdá, adding that he believes the Trump administration deserves blame for that loss of trust.

When Vos’ colleagues analyzed the variation in COVID-19 infection and infection-fatality ratios among 177 countries, they surprisingly found that pandemic preparedness did not have an effect but measures of trust in government and trust in other people — and of government corruption — did. By their reckoning, if the trust in government levels in other countries matched those in Denmark, there would have been 13% fewer infections in the world, and if interpersonal trust was at Danish levels, there would have been 40% fewer infections.

Wilson sees the trust problem as extending well beyond the CDC and public health and as predating the Trump administration. He refers to the amount of money people are putting into cryptocurrency as an example. “The rise of cryptocurrency is not just because people are greedy and want to make money,” he says. “It’s also because a lot of people think it’s like private money.”

Wilson says when he teaches undergraduates at Brown, he tries to get across that healthcare systems are not separate and they reflect the values and beliefs of the societies they serve.

“(The U.S. has) a deeply divided society” he says. “Solving all these problems (must) be addressed at the same time. People aren’t going to take vaccinations just because we invest in public health.”

Peter Wehrwein is managing editor of Managed Healthcare Executive.
The Next Era in Oncology Care Management: Clinicians Are Consumers

The future of oncology care is going beyond traditional care management by bringing an agile, patient-first approach to traditional models. This approach empowers clinicians to not just monitor patients, but also actively guide them. Jasper Health embodies this model: members are given options and context about how to manage their health and clinicians are equipped with powerful data and insights to actively manage care.

Clinician-empowered, patient-centered care
To date, most care management platforms have focused on workflows and repeatable processes that are delivered using outdated interfaces and centralized platform design approaches. Very few solutions or processes are created with a singular focus on cancer and how it uniquely affects members and their clinicians. Integration is key to engagement, the experience, and creating a holistic approach that delivers whole-person care focused on clinical, functional, emotional, and psychosocial status. Jasper Health was created on a consumer-centric approach that organically drives engagement and delivers on the most unique set of real-time member-reported outcomes in the industry. The same consumer-centric design also serves clinicians as an extension of support for clinical care team partners, optimizing early interventions and enhanced management of care which is shown to better outcomes for members.

Clinicians are consumers
Well-meaning solutions often compromise the patient experience, and the traditional Health IT industry typically puts the clinical team user experience as a low priority which adds to clinical burnout and frustration. Jasper Health leveraged its executive team’s extensive healthcare experience and consumer expertise with brands like Lyft, Trulia, and Fitbit to craft a patient-centered and clinically-empowering experience for oncology care. Jasper Care+, the first clinician-as-a-consumer care guiding and management experience, leverages continuous learning to produce a sophisticated dashboard and clinical engagement engine. The process delivers only the most critical alerts while implementing the learned behavior and member journey to automate those lower priority tasks. This reduces “alert fatigue,” so clinical care teams can easily prioritize and act upon information.

The first psychosocial exception-based triage dashboard for clinicians
Traditionally, triage dashboards surfaced clinical variables stratified red, yellow, green for care managers to prioritize who needs help now versus in the future.

This traditional format serves purely clinical use cases leaving out the rest of the story when it comes to a complete whole person illustration of the patient. Jasper Care+ is the first triage dashboard that incorporates not only the clinical data elements but psychosocial ePROs like mental health, diet and nutrition, financial issues, and physical activity. Moreover, Jasper Care+ incorporates biometric devices, like Fitbit and Apple Health, to bring in passive lifestyle biometrics as well as other data types to provide the most unique view of a member’s current health status and subjective concerns.

A Powerful Solution
• Over 13,000 members served on the platform today with 68% reporting less stress and anxiety and 78% reporting improved medication adherence
• Care professional orchestration allows custom rules for routing member requests
• Smart nudges to patients based on their behavior, diagnosis, treatment plan, and journey
• Adjustable risk stratification for organization specific clinical protocols recorded
• HiPAA-compliant asynchronous and video virtual care capabilities
• Flexible platform that seamlessly integrates versus creating replacement expenses

Adam Pellegrini
CEO and Co-Founder

Adam Pellegrini is CEO and Co-Founder of Jasper Health. With digital application experience at CVS, Fitbit, Walgreens, Microsoft, The American Cancer Society, and as a clinician in the U.S. Army, Adam’s 27 years of diverse experience across multiple sectors drive his empathetic, patient-driven approach to helping those with cancer.

Visit hellojasper.com to request a conversation about how Jasper Health can improve the cancer care experience and reduce costs.

New research shows a wide gap between what health systems say is value-based care and how physicians are compensated. The research is significant because the Affordable Care Act (ACA) and dozens of other programs and policies in both the public and private sector are supposed to be ushering in a new era in U.S. healthcare that relegates fee for service, which incentivizes provision of services, to the past and replaces it with payment arrangements that reward outcomes and lower costs.

This study is also important because the researchers noted they could not find any earlier study that specifically focused on the compensation and financial incentives health systems use when paying physicians. However, research findings published on Jan. 28, 2022, in *JAMA Health Forum* show that the physician compensation arrangements at the 22 health systems included in the study still center on increasing the number of healthcare services that physicians deliver.

Researchers at RAND Corporation analyzed the payment practices that 31 physician organizations affiliated with 22 health systems in California, Minnesota, Wisconsin and Washington used with their frontline physicians. They found the payment methods were designed to maximize health system revenue by incentivizing doctors to deliver more services. Specifically, the volume-based compensation was the most common component of the primary care physicians’ (PCPs) base compensation in 26 physician organizations, representing an average of 68.2% of total compensation for PCPs. In 29 physician groups, volume-based compensation represented an average of 73.7% of total compensation for specialists, the researchers reported.

In recent years, many health systems have acquired physician organizations in an effort to control referrals to their hospitals and other facilities. Therefore, compensation and financial incentives are a lever for health systems to affect how physicians deliver care, the researchers noted. Health systems have also started to adopt alternative payment models (APMs) — just as health plans and CMS have done. "Given increased exposure of health systems to APMs, it is important to understand the degree to which health system compensation and incentives for physicians reflect the same value-based incentives provided by payers," the researchers wrote.

Although financial incentives for delivering high-quality clinical care, lowering costs and improving patients’ experience with access to care were commonly included in compensation for PCPs and specialty physicians, those payments represented only a small fraction of total compensation. As a result, those payments were likely to only slightly affect physician behavior, the researchers noted. The research shows that just over two-thirds (70%) of the leaders of physician organizations that the researchers interviewed said increasing the volume of services delivered was the main way for physicians to boost their income.

Dennis P. Scanlon, Ph.D., a health policy professor at Pennsylvania State University in State College, says health systems are still largely using discounted fee-for-service reimbursement methods. Since even before the ACA was passed in 2010, health systems have developed various alternative payment mechanisms, such as capitation for accountable care organizations, episode-based contracts and bundled payments for care, he explains. Scanlon says value-based payment schemes may sound great in marketing pro-
grams, “but at the end of the day, we still see rising healthcare costs in part because of the incentives to increase volume.”

The American Academy of Family Physicians defines value-based payments as systems in which health insurers and government and employer purchasers of healthcare hold physicians, hospitals and other providers accountable for both the quality of care they deliver and the cost of that care. Health policy experts at Dell Medical School of the University of Texas at Austin have a more detailed definition. “Value in healthcare is the measured improvement in a person’s health outcomes for the cost of achieving that improvement,” Elizabeth Teisberg, Ph.D., and colleagues wrote in an article that was published in 2020. Some descriptions of value-based care conflated it with cost reduction, quality improvement or patient satisfaction, Teisberg and colleagues wrote. Such efforts are important, but they are not the same as delivering value. Improved patient outcomes will result in reduced costs, they added.

Teisberg is the executive director of the Value Institute for Health and Care at Dell Medical School, and she co-authored “Redefining Health Care: Creating Value-based Competition on Results,” with Michael E. Porter. That book, which was published in 2006, popularized some of the underlying ideas of value-based care.

Mark Bethke, an actuary and leader of Deloitte Consulting’s value-based care practice, says most health systems are reluctant to invest sufficient funds in value-based care payment models to provide enough of an incentive for physicians to improve patients’ health outcomes. Bethke has worked with Deloitte’s health system clients on value-based care programs since 1999. “What I learned over those years is that most value-based payment models fail without making other significant changes to the care delivery model,” he says. For example, health systems do not put enough payment at risk because they fear investing too much in value-based care will cannibalize their fee-for-service revenue, he explains.

Most health systems put only about 5% of total revenue at risk in value-based contracts with physicians, he says. “Then after two or three years, they’ll say it didn’t work because patient outcomes didn’t improve and costs didn’t go down,” Bethke says. “It’s foolish to invest just 5% of your overall revenue in value-based care.” The ideal level is more like 40%, which he calls the tipping point, where value-based contracts represent enough of a commitment so the payment eventually results in a return on the investment in terms of improved outcomes and lower costs.

Putting only 5% into value-based contracts does not provide enough of a financial incentive for physicians and other providers to manage the total cost of care, Bethke explains. Without a more robust investment of 40%, health systems disconnect their goals of delivering value-based care from the way physicians deliver care.

Rachel O. Reid, M.D., M.S., the lead author on the JAMA Health Forum article, agreed and says health systems and provider organizations will need to evolve the way they pay physicians who treat patients to align with value-based care delivery models. Otherwise, the nation’s health system may not realize the potential of value-based payment reform to deliver better value for patients. Reid is a physician policy researcher at RAND and a practicing internal medicine PCP at Brigham and Women’s Hospital in Boston. “It’s important to acknowledge and be aware of the disconnect that exists at the interface between a payer or insurer and a provider organization, and then between the provider organization and the frontline physicians,” she says. “Some of the rhetoric about value-based care might not match what’s happening among frontline doctors, where the rubber hits the road.”

Joseph Burns is an independent journalist in Brewster, Massachusetts, who covers healthcare and healthcare insurance.
LIBTAYO works with the immune system to help treat the following types of cancer:

- The first-line treatment of patients with non–small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression (tumor proportion score [TPS] ≥50%) as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations, and is locally advanced where patients are not candidates for surgical resection or definitive chemoradiation OR metastatic.
- The treatment of patients with locally advanced basal cell carcinoma (laBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.
- For the treatment of patients with metastatic BCC (mBCC) previously treated with an HHI or for whom an HHI is not appropriate. The mBCC indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for mBCC may be contingent upon verification and description of clinical benefit.
- The treatment of patients with metastatic cutaneous squamous cell carcinoma (mCSCC) or locally advanced CSCC (laCSCC) who are not candidates for curative surgery or curative radiation.

Visit LIBTAYOhcp.com for more information.

**Important Safety Information**

**Warnings and Precautions**

**Severe and Fatal Immune-Mediated Adverse Reactions**

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue at any time after starting treatment. While immune-mediated adverse reactions usually occur during treatment, they can also occur after discontinuation. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. Early identification and management are essential to ensuring safe use of PD-1/PD-L1–blocking antibodies. The definition of immune-mediated adverse reactions included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.
Important Safety Information (cont’d)

Warnings and Precautions (cont’d)

Severe and Fatal Immune-Mediated Adverse Reactions (cont’d)

No dose reduction for LIBTAYO® is recommended. In general, withhold LIBTAYO® for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue LIBTAYO® for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Withhold or permanently discontinue LIBTAYO® depending on severity. In general, if LIBTAYO® requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Immune-mediated pneumonitis: LIBTAYO® can cause immune-mediated pneumonitis. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.2% (25/810) of patients receiving LIBTAYO®, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%). Pneumonitis led to permanent discontinuation in 1.4% of patients and withholding of LIBTAYO® in 2.1% of patients. Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO® was withheld, 9 reinitiated after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis. Withhold LIBTAYO® for Grade 2, and permanently discontinue for Grade 3 or 4.

Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated colitis: LIBTAYO® can cause immune-mediated colitis. The primary component of immune-mediated colitis was diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory immune-mediated colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO®, including Grade 3 (0.9%) and Grade 2 (1.1%). Colitis led to permanent discontinuation in 0.4% of patients and withholding of LIBTAYO® in 1.5% of patients. Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO® was withheld, 9 reinitiated after symptom improvement; of these, 3/9 (75%) had recurrence. Withhold LIBTAYO® for Grade 2 or 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated hepatitis: LIBTAYO® can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO®, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%). Hepatitis led to permanent discontinuation of LIBTAYO® in 1.2% of patients and withholding of LIBTAYO® in 0.5% of patients. Systemic corticosteroids were required in all patients with hepatitis. Additional immunosuppression with mycophenolate was required in 19% (3/16) of these patients. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO® was withheld, 3 reinitiated LIBTAYO® after symptom improvement; of these, none had recurrence.

For hepatitis with no tumor involvement of the liver: Withhold LIBTAYO® if AST or ALT increases to more than 3 and up to 8 times the upper limit of normal (ULN) or if total bilirubin increases to more than 1.5 and up to 3 times the ULN. Permanently discontinue LIBTAYO® if AST or ALT increases to more than 8 times the ULN or total bilirubin increases to more than 3 times the ULN.

For hepatitis with tumor involvement of the liver: Withhold LIBTAYO® if baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN. Also, withhold LIBTAYO® if baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN. Permanently discontinue LIBTAYO® if AST or ALT increases to more than 10 times ULN or if total bilirubin increases to more than 3 times ULN. If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue LIBTAYO® based on recommendations for hepatitis with no liver involvement.

Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated endocrinopathies: For Grade 3 or 4 endocrinopathies, withhold until clinically stable or permanently discontinue depending on severity.

• Adrenal insufficiency: LIBTAYO® can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO® depending on severity. Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO®, including Grade 3 (0.4%). Adrenal insufficiency led to permanent discontinuation of LIBTAYO® in 1 (0.1%) patient. LIBTAYO® was not withheld in any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff.

Please see additional Important Safety Information and Brief Summary of Prescribing Information on the following pages.
Important Safety Information (cont’d)

Warnings and Precautions (cont’d)

Severe and Fatal Immune-Mediated Adverse Reactions (cont’d)

Immune-mediated endocrinopathies: (cont’d)

• **Hypophysitis:** LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue depending on severity. Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) of patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff.

• **Thyroid disorders:** LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity.

• **Thyroiditis:** Thyroiditis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including Grade 2 (0.2%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis had not resolved in any patient at the time of data cutoff. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported.

• **Hyperthyroidism:** Hyperthyroidism occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 2 (0.9%). No patient discontinued treatment and LIBTAYO was withheld in 0.5% of patients due to hyperthyroidism. Systemic corticosteroids were required in 3.8% (1/26) of patients. Hyperthyroidism resolved in 50% of 26 patients. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism.

• **Hypothyroidism:** Hypothyroidism occurred in 7% (60/810) of patients receiving LIBTAYO, including Grade 2 (6%). Hypothyroidism led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. Hypothyroidism led to withholding of LIBTAYO in 1.1% of patients. Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 8.3% of the 60 patients. Majority of the patients with hypothyroidism required long-term thyroid hormone replacement. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy.

• **Type 1 diabetes mellitus, which can present with diabetic ketoacidosis:** Monitor for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity. Type 1 diabetes mellitus occurred in 0.1% (1/810) of patients, including Grade 4 (0.1%). No patient discontinued treatment due to type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients.

**Immune-mediated nephritis with renal dysfunction:** LIBTAYO can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 3 (0.1%), and Grade 2 (0.4%). Nephritis led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 0.4% of patients. Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 80% of the 5 patients. Of the 3 patients in whom LIBTAYO was withheld, 2 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence. Withhold LIBTAYO for Grade 2 or 3 increased blood creatinine, and permanently discontinue for Grade 4 increased blood creatinine. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

**Immune-mediated dermatologic adverse reactions:** LIBTAYO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1–blocking antibodies. Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%). Immune-mediated dermatologic adverse reactions led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients. Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 69% of the 13 patients. Of the 11 patients in whom LIBTAYO was withheld for dermatologic adverse reactions, 7 reinitiated LIBTAYO after symptom improvement; of these, 43% (3/7) had recurrence of the dermatologic adverse reaction. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold LIBTAYO for suspected SJS, TEN, or DRESS. Permanently discontinue LIBTAYO for confirmed SJS, TEN, or DRESS. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

**Other immune-mediated adverse reactions:** The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in 810 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

• **Cardiac/vascular:** Myocarditis, pericarditis, and vasculitis. Permanently discontinue for Grades 2, 3, or 4 myocarditis.

• **Nervous system:** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, and autoimmune neuropsychopathy. Withhold for Grade 2 neurological toxicities and permanently discontinue for Grades 3 or 4 neurological toxicities. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.
Important Safety Information (cont’d)

Warnings and Precautions (cont’d)

Severe and Fatal Immune-Mediated Adverse Reactions (cont’d)

Other immune-mediated adverse reactions: (cont’d)

- **Ocular**: Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss.

- **Gastrointestinal**: Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis.

- **Musculoskeletal and connective tissue**: Myositis/polymyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica.

- **Endocrine**: Hypoparathyroidism.

- **Other (hematologic/immune)**: Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection.

Infusion-related reactions

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash and dyspnea. Interrupt or slow the rate of infusion for Grade 1 or 2, and permanently discontinue for Grade 3 or 4.

Complications of allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/ PD-L1–blocking antibody prior to or after an allogeneic HSCT.

Embryo-fetal toxicity

LIBTAYO can cause fetal harm when administered to a pregnant woman due to an increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

Adverse Reactions

- In the pooled safety analysis of 810 patients, the most common adverse reactions (≥15%) with LIBTAYO were musculoskeletal pain, fatigue, rash, and diarrhea.

- In the pooled safety analysis of 810 patients, the most common Grade 3-4 laboratory abnormalities (≥2%) with LIBTAYO were lymphopenia, hyponatremia, hypophosphatemia, increased aspartate aminotransferase, anemia, and hyperkalemia.

Use in Specific Populations

- **Lactation**: Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

- **Females and males of reproductive potential**: Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO.

Please see Brief Summary of Prescribing Information on the following pages.

ALK, anaplastic lymphoma kinase; EGFR, epidermal growth factor receptor; FDA, US Food and Drug Administration; PD-L1, programmed death ligand-1; ROS1, c-ros oncogene 1 receptor tyrosine kinase.


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LIBTAYO® (cemiplimab-rwlc) injection, for intravenous use

Brief Summary of Prescribing Information

1 INDICATIONS AND USAGE

1.1 Cutaneous Squamous Cell Carcinoma

LIBTAYO is indicated for the treatment of patients with metastatic cutaneous squamous cell carcinoma (mSCC) or locally advanced SCC (lSCC) who are not candidates for curative surgery or curative radiation.

1.2 Basal Cell Carcinoma

LIBTAYO is indicated for the treatment of patients:

- with locally advanced basal cell carcinoma (lbBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate.
- with metastatic BCC (mBCC) previously treated with a hedgehog pathway inhibitor or for whom a hedgehog pathway inhibitor is not appropriate. The mBCC indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for the mBCC indication may be contingent upon verification and description of clinical benefit.

1.3 Non-Small Cell Lung Cancer

LIBTAYO is indicated for the first-line treatment of patients with non-small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [Tumor Proportion Score (TPS) ≥ 50%] as determined by an FDA-approved test [see Dosage and Administration (2.1) in the full prescribing information], with no EGFR, ALK or ROS1 aberrations, and is:

- locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or
- metastatic.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Severe and Fatal Immune-Mediated Adverse Reactions

LIBTAYO is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death receptor-1 (PD-1) or PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies. Immune-mediated adverse reactions affecting more than one body system can occur simultaneously.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information]. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Immune-Mediated Pneumonitis

LIBTAYO can cause immune-mediated pneumonitis. The definition of immune-mediated pneumonitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. In patients treated with other PD-1/PD-L1 blocking antibodies the incidence of pneumonitis is higher in patients who have received prior thoracic radiation.

Immune-mediated pneumonitis occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%) adverse reactions. Pneumonitis led to permanent discontinuation of LIBTAYO in 1.4% of patients and withholding of LIBTAYO in 2.1% of the patients.

Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO was withheld for pneumonitis, 9 reinitiated LIBTAYO after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis.

Immune-Mediated Colitis

LIBTAYO can cause immune-mediated colitis. The definition of immune-mediated colitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. The primary component of the immune-mediated colitis was diarrhea.

Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1 blocking antibodies. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (1.1%) adverse reactions. Colitis led to permanent discontinuation of LIBTAYO in 0.4% of patients and withholding of LIBTAYO in 1.5% of patients.

Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO was withheld for colitis, 4 reinitiated LIBTAYO after symptom improvement; of these, 3/4 (75%) had recurrence of colitis.

Immune-Mediated Hepatitis

LIBTAYO can cause immune-mediated hepatitis. The definition of immune-mediated hepatitis included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology.

Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%) adverse reactions. Hepatitis led to permanent discontinuation of LIBTAYO in 1.2% of patients and withholding of LIBTAYO in 0.5% of patients.

Systemic corticosteroids were required in all patients with hepatitis. Nineteen percent (19%) of these patients (3/16) required additional immunosuppression with mycophenolate. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO was withheld for hepatitis, 3 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hepatitis.

Immune-Mediated Endocrinopathies

Adrenal Insufficiency

LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information].

Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.4%) adverse reactions. Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. LIBTAYO was not withheld in any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff.

Hypophysitis

LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information].
Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff.

**Thyroid Disorders**

LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathies. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity [see Dosage and Administration (2.3) in the full prescribing information].

Thyroiditis: Thyroiditis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including Grade 2 (0.2%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis had not resolved in any patient at the time of data cutoff. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported.

**Immune-Mediated Adverse Reactions**

**5.1 Severe and Fatal Immune-Mediated Adverse Reactions**

None.

**5.2 Infusion-Related Reactions**

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash and dyspnea.

**5.3 Complications of Allogeneic HSCT**

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

**5.4 Embryo-Fetal Toxicity**

Based on its mechanism of action, LIBTAYO can cause fetal harm when administered to a pregnant woman. Animal studies have demonstrated that inhibition of the PD-1/PD-L1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose [see Use in Specific Populations (8.1, 8.3)].

**6 ADVERSE REACTIONS**

The following serious adverse reactions are described elsewhere in the labeling.

- Severe and Fatal Immune-Mediated Adverse Reactions [see Warnings and Precautions (5.1)]
1. Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data described in Warnings and Precautions reflect exposure to LIBTAYO as a single agent in 810 patients in three open-label, single-arm, multicohort studies (Study 1423, Study 1540 and Study 1620), and one open-label randomized multi-center study (Study 1624). These studies included 219 patients with advanced CSCC (Studies 1540 and 1423), 132 patients with advanced BCC (Study 1620), 355 patients with NSCLC (Study 1624), and 104 patients with other advanced solid tumors (Study 1425). LIBTAYO was administered intravenously at doses of 3 mg/kg every 2 weeks (n=235), 350 mg every 3 weeks (n=543), or other doses (n=32; 1 mg/kg every 2 weeks, 10 mg/kg every 2 weeks, 200 mg every 2 weeks). Among the 810 patients, 57% were exposed for ≥6 months and 22% were exposed for ≥12 months. In this pooled safety population, the most common adverse reactions (≥15%) were musculoskeletal pain, fatigue, rash, and diarrhea. The most common Grade 3-4 laboratory abnormalities (≥2%) were lymphopenia, hyponatremia, hypophosphatemia, increased aspartate aminotransferase, anemia, and hyperkalemia.

Cutaneous Squamous Cell Carcinoma (CSCC)

The safety of LIBTAYO was evaluated in 219 patients with advanced CSCC (metastatic or locally advanced disease) in Study 1423 and Study 1540 [see Clinical Studies (14.1) in the full prescribing information]. Of these 219 patients, 131 had mCSCC (nodal or distant) and 88 had laCSCC. Patients receiving LIBTAYO 1 mg/kg every 2 weeks (n=11), 3 mg/kg every 2 weeks (n=162) or 350 mg every 3 weeks (n=56) as an intravenous infusion until disease progression, unacceptable toxicity, or completion of planned treatment. The median duration of exposure was 38 weeks (2 weeks to 110 weeks).

The safety population characteristics were: median age of 72 years (38 to 96 years), 83% male, 96% White, and European Cooperative Oncology Group (ECOG) performance score (PS) of 0 (44%) and 1 (56%). Serious adverse reactions occurred in 35% of patients. Serious adverse reactions that occurred in at least 2% of patients were pneumonitis, cellulitis, sepsis, and pneumonia.

Permanent discontinuation due to an adverse reaction occurred in 8% of patients. Adverse reactions resulting in permanent discontinuation were pneumonitis, cough, pneumonia, encephalitis, aseptic meningitis, hepatitis, arthralgia, muscular weakness, neck pain, soft tissue necrosis, complex regional pain syndrome, lefthargy, paresthesia, rash maculopapular, pruritus, and confusional state.

The most common (≥20%) adverse reactions were fatigue, rash, diarrhea, musculoskeletal pain, and nausea. The most common Grade 3 or 4 adverse reactions (≥2%) were cellulitis, anemia, hypertension, pneumonia, musculoskeletal pain, fatigue, pneumonitis, sepsis, skin infection, and hypercalcemia. The most common (≥4%) Grade 3 or 4 laboratory abnormalities worsening from baseline to Grade 3 or 4 were lymphopenia, anemia, hypotremicemia, and hypophosphatemia.

Table 2 summarizes the adverse reactions that occurred in ≥10% of patients and Table 3 summarizes Grade 3 or 4 laboratory abnormalities worsening from baseline in ≥1% of patients receiving LIBTAYO.

### Table 2: Adverse Reactions in ≥10% of Patients with Advanced CSCC Receiving LIBTAYO in Study 1423 and Study 1540

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>LIBTAYO N=219</th>
<th>All Grades</th>
<th>Grades 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General and Administration Site</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>34</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td><strong>Skin and Subcutaneous Tissue</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>31</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>18</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>25</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>21</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>13</td>
<td>0.5</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>10</td>
<td>0.5</td>
<td></td>
</tr>
</tbody>
</table>

(continued)

### Table 3: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in ≥1% of Patients with Advanced CSCC Receiving LIBTAYO in Study 1423 and Study 1540

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>Grade 3-4 (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemistry</td>
<td></td>
</tr>
<tr>
<td>Increased aspartate aminotransferase</td>
<td>2</td>
</tr>
<tr>
<td>Increased INR</td>
<td>2</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>9</td>
</tr>
<tr>
<td>Anemia</td>
<td>5</td>
</tr>
<tr>
<td>Electrolytes</td>
<td></td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1.5</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>3.1</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>4</td>
</tr>
<tr>
<td>Hypercalcemia</td>
<td>2</td>
</tr>
</tbody>
</table>

Toxicity graded per NCI CTCAE v. 4.03

- a. Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter.

Basal Cell Carcinoma (BCC)

The safety of LIBTAYO was evaluated in 132 patients with advanced BCC (mBCC N=48, laBCC N=84) in an open-label, single-arm trial (Study 1620) [see Clinical Studies (14.2) in the full prescribing information]. Patients received LIBTAYO 350 mg every 3 weeks as an intravenous infusion for up to 93 weeks or until disease progression or unacceptable toxicity. The median duration of exposure was 42 weeks (range: 2.1 weeks to 94 weeks).

The safety population characteristics were: median age of 68 years (38 to 90 years), 67% male, 74% White, and ECOG performance score (PS) of 0 (62%) and 1 (38%).

Serious adverse reactions occurred in 32% of patients. Serious adverse reactions that occurred in >1.5% (at least 2 patients) were urinary tract infection, colitis, acute kidney injury, adrenal insufficiency, anemia, infected neoplasm, and somnolence. Fatal adverse reactions occurred in 1.5% of patients who received LIBTAYO, including acute kidney injury and cachexia.

Permanently discontinued LIBTAYO due to an adverse reaction occurred in 13% of patients. Adverse reactions resulting in permanent discontinuation of LIBTAYO in >1.5% (at least 2 patients) were colitis and general physical health deterioration.

Dosage delays of LIBTAYO due to an adverse reaction occurred in 34% of patients. Adverse reactions which required dosage delay in >2% of patients (at least 3 patients) included blood creatinine increased, diarrhea, colitis, fatigue, headache, pneumonitis, and urinary tract infection.
The most common adverse reactions reported in at least 15% of patients were fatigue, musculoskeletal pain, diarrhea, rash, pruritus, and upper respiratory tract infection. The most common Grade 3 or 4 adverse reactions (>2%) were hypertension, colitis, fatigue, urinary tract infection, pneumonia, increased blood pressure, hypokalemia, and visual impairment. The most common (>3%) laboratory abnormality worsening from baseline to Grade 3 or 4 was hyponatremia.

Table 4 summarizes the adverse reactions that occurred in ≥10% of patients and Table 5 summarizes Grade 3 or 4 laboratory abnormalities worsening from baseline in ≥1% of patients receiving LIBTAYO.

Table 4: Adverse Reactions in ≥10% of Patients with Advanced BCC Receiving LIBTAYO in Study 1620

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>LIBTAYO N=322</th>
<th>All Grades</th>
<th>Grades 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders and administration site conditions</td>
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<td></td>
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</tr>
<tr>
<td>Fatigue</td>
<td>35</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>33</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>25</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>12</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>11</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>22</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>20</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>15</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>12</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>14</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>13</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>12</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>11</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Vascular disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>11</td>
<td>4.5</td>
<td></td>
</tr>
</tbody>
</table>

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v.4.03

a. Composite term includes fatigue, asthenia, and malaise
b. Composite term includes arthralgia, back pain, myalgia, pain in extremity, musculoskeletal pain, neck pain, musculoskeletal stiffness, musculoskeletal chest pain, musculoskeletal discomfort, and spinal pain
c. Composite term includes rash maculo-papular, rash, dermatitis, dermatitis acniform, erythema, rash pruritic, dermatitis bullous, dyschidrotic eczema, pemphigoid, rash erythematous, and urticaria
d. Composite term includes upper respiratory tract infection, nasopharyngitis, rhinitis, sinusitis, pharyngitis, respiratory tract infection, and viral upper respiratory tract infection
e. Composite term includes dyspnea and dyspnea exertional
f. Composite term includes hypertension and hypertensive crisis

Table 5: Grade 3 or 4 Laboratory Abnormalities Worsening from Baseline in ≥1% of Patients with Advanced BCC Receiving LIBTAYO in Study 1620

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>Grade 3-4 (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrolytes</td>
<td></td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>3.1</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>1.5</td>
</tr>
<tr>
<td>Coagulation</td>
<td></td>
</tr>
<tr>
<td>Activated partial thromboplastin time prolonged</td>
<td>2.3</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
</tr>
<tr>
<td>Lymphocyte count decreased</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Toxicity graded per NCI CTCAE v.4.03

a. Percentages are based on the number of patients with at least 1 post-baseline value available for that parameter

Non-Small Cell Lung Cancer (NSCLC)

The safety of LIBTAYO was evaluated in 355 patients with locally advanced or metastatic NSCLC in Study 1624 [see Clinical Studies (14.3) in the full prescribing information]. Patients received LIBTAYO 350 mg every 3 weeks (n=355) or investigator’s choice of chemotherapy (n=342), consisting of pemetrexed plus cisplatin or carboplatin; gemcitabine plus cisplatin or carboplatin; or pemetrexed plus cisplatin or carboplatin followed by optional pemetrexed maintenance. The median duration of exposure was 27.3 weeks (9 days to 115 weeks) in the LIBTAYO group and 17.7 weeks (18 days to 86.7 weeks) in the chemotherapy group. In the LIBTAYO group, 54% of patients were exposed to LIBTAYO for ≥6 months and 22% were exposed for ≥12 months.

The safety population characteristics were: median age of 63 years (31 to 79 years), 44% of patients 65 or older, 88% male, 86% White, 82% had metastatic disease and 18% had locally advanced disease and ECOG performance score (PS) of 0 (27%) and 1 (73%).

LIBTAYO was permanently discontinued due to adverse reactions in 8% of patients; adverse reactions resulting in permanent discontinuation in at least 2 patients were pneumonitis, pneumonia, ischemic stroke and increased aspartate aminotransferase. Serious adverse reactions occurred in ≥28% of patients. The most frequent serious adverse reactions in ≥2% of patients were pneumonia and pneumonitis.

Table 6 summarizes the adverse reactions that occurred in ≥10% of patients and Table 7 summarizes Grade 3 or 4 laboratory abnormalities in patients receiving LIBTAYO.

Table 6: Adverse Reactions in ≥10% of Patients with Locally Advanced or Metastatic NSCLC Receiving LIBTAYO in Study 1624

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>LIBTAYO N=355</th>
<th>All Grades</th>
<th>Grades 3-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>26</td>
<td>0.6</td>
<td>27</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>15</td>
<td>1.4</td>
<td>6</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>15</td>
<td>3.4</td>
<td>50</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>14</td>
<td>1.1</td>
<td>26</td>
</tr>
<tr>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>12</td>
<td>0.6</td>
<td>18</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>11</td>
<td>5</td>
<td>12</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>11</td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NI CTCAE) v.4.03

a. Musculoskeletal pain is a composite term that includes back pain, arthralgia, pain in extremity, musculoskeletal pain, chest pain, bone pain, myalgia, neck pain, spinal pain, and musculoskeletal stiffness
b. Rash is a composite term that includes rash, dermatitis, urticaria, rash maculo-papular, erythema, rash erythematous, rash pruritic, psoriasis, autoimmune dermatitis, dermatitis acniform, dermatitis allergic, dermatitis atopc, dermatitis bullous, drug eruption, dyschidrotic eczema, lichen planus, and skin reaction
c. Fatigue is a composite term that includes fatigue, asthenia, and malaise
d. Pneumonia is a composite term that includes atypical pneumonia, embolic pneumonia, lower respiratory tract infection, lung abscess, paracancerous pneumonia, pneumonia, pneumonia bacterial, and pneumonia klesobsita
e. Cough is a composite term that includes cough and productive cough
In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 10% to 20%, respectively.

**Data**

**Animal Data**

Animal reproduction studies have not been conducted with LIBTAYO to evaluate its effect on reproduction and fetal development. A central function of the PD-1/PD-L1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to the fetus. In murine models of pregnancy, blockade of PD-L1 signaling has been shown to disrupt tolerance to the fetus and to result in an increase in fetal loss; therefore, potential risks of administering LIBTAYO during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD-1/PD-L1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PD-1 and PD-L1 knockout mice. Based on its mechanism of action, fetal exposure to cemiplimab-rwlc may increase the risk of developing immune-mediated disorders or altering the normal immune response.

**6.2 Lactation**

**Risk Summary**

There is no information regarding the presence of cemiplimab-rwlc in human milk, or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO.

**8.3 Females and Males of Reproductive Potential**

**Pregnancy Testing**

Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO [see Use in Specific Populations (8.1)].

**Contraception**

LIBTAYO can cause fetal harm when administered to a pregnant woman [see Use in Specific Populations (8.1)].

**Females**

Advises females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose. No overall differences in safety or effectiveness were observed between these patients and younger patients.

**8.4 Pediatric Use**

The safety and effectiveness of LIBTAYO have not been established in pediatric patients.

**8.5 Geriatric Use**

Of the 810 patients who received LIBTAYO in clinical studies, 32% were 65 years up to 75 years and 22% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients. Of the 219 patients with mCSCC or laCSCC who received LIBTAYO in clinical studies, 34% were 65 years up to 75 years and 41% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients. Of the 132 patients with BCC who received LIBTAYO in Study 1620, 27% were 65 years up to 75 years, and 32% were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

**REGENERON | SANOFI GENZYME**

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Lib.21.06.0104 07/21
Fabric Health is bringing healthcare services to laundromats in Philadelphia and Pittsburgh. Other organizations are using barbershops and churches to deliver healthcare services and messages. by SUSAN LADIKA

Fabric Health is, you might say, working to do its part to wash away health disparities by offering residents in Philadelphia, access to healthcare services at laundromats.

The idea behind Fabric Health is to “meet busy families where they are,” says co-founder Courtney Bragg, MBA. 

Along with washing and drying their clothes, customers at five Philadelphia laundromats have been able to sign up for health insurance, get a mammogram, undergo a skin cancer screening or get a blood test for liver cancer or hepatitis B. Bragg says laundromats are “de facto community centers,” as many customers show up weekly to wash their clothes.

Fabric Health is one of a number of efforts that move healthcare communication and some service delivery to unusual settings. Other groups have found ways of using barbershops and churches.

Bragg and co-founder Allister Chang were introduced by friends over a year ago. They had both spent a lot of time at laundromats, and together, they dreamed up the idea for Fabric Health, a for-profit social impact startup. They then spent time talking to healthcare leaders to “understand their pain points,” Bragg says.

Bragg has experience in education and healthcare, and Chang is a member of the Washington, D.C., State Board of Education and has worked with various nonprofits, including four years as executive director of Libraries Without Borders. Over the years, the pair had gotten to know Brian Holland, co-owner of The Laundry Café, and they launched Fabric Health out of The Laundry Café’s five locations in North and West Philadelphia. The founders received grants and investments to start their venture.

Before launching, they visited laundromats and talked to people as they helped them wash and fold their clothes. “You can’t just parachute in and parachute out and expect people are going to trust you and talk to you,” Bragg says.

If healthcare inequity is the problem, then Philadelphia is a good place to test solutions. The city is the poorest large city in the United States. One in 4 of Philadelphia’s households lives below the federal poverty line.

The Fabric Health founders learned through their discussions with healthcare experts that more than 100,000 Philadelphians did not have health insurance. One of their first moves was handing out flyers to laundromat customers, asking whether they knew anyone who was uninsured. Bragg and Chang also directly talked to people — and got an earful amid the din of the washers and dryers. So, they connected with Pennie, the state’s health insurance marketplace, to provide information and help laundromat customers sign up for health insurance coverage. Consumers are “inundated with information” about insurance, Bragg says, but they don’t know how to sort through it. Bragg and Chang recognized an opportunity to introduce Pennie to the uninsured and answer people’s questions. They even got Pennie’s Executive Director Zachary Sherman to attend an in-person question-and-answer session at the laundromat.

Sherman says he welcomed the chance to connect with those who may not be aware of their insurance coverage options. “Disproportionately, they tend to be in communities of color. They tend to be lower income,” he says. Many of the uninsured qualify for Medicaid or for coverage through Pennie at low or no cost, Sherman explains. Taking advantage of the time people have
on their hands at a laundromat is a "really cool (and) interesting idea," Sherman says.

Bragg and Chang also connected with Jefferson Health, a large health system that competes with Penn Medicine in the Philadelphia market. Jefferson Health has an RV that is equipped to do mobile cancer screenings, including 3D mammograms. With the RV, Jefferson Health has offered free mammograms and other cancer screenings at Fabric Health locations.

Amy Leader, Dr.Ph., M.P.H., an associate professor of public health at Thomas Jefferson University who leads the mobile cancer screening efforts, calls the RV "one of our crown jewels," allowing the health system to do screenings at libraries, churches and community centers. — and laundromats.

Fabric Health has started to expand. With a $500,000 grant from the Richard King Mellon Foundation, it is going to open up business in Pittsburgh.

Barbershops and churches
In 2019, The University of Texas at Austin School of Nursing, with support from the city of Austin, began providing mental health and wellness care at two Black churches in a program called African American Mental Health and Wellness Program (AMEN). Part of the goal is to combat the stigma surrounding mental health issues in the Black community. Initially, the program provided training for pastors who "sometimes felt ill-equipped to handle" church members with mental health issues, and they received information on when and where to refer people for further care, explains Jacklyn Hecht, managing director of the project.

When COVID-19 hit, the program became remote. As many people were left feeling isolated at home, the nursing school worked with the pastors to develop an outreach program. Healthcare workers also called congregants to see how they were faring. "With (COVID-19), no one has been immune from having some kind of mental health stress," Hecht says.

"Members just wanted to talk," says Angela Bigham, a community health worker the University of Texas, who is involved with AMEN at her church, Rehoboth Baptist, in Austin. If people were troubled, the pastor would be notified so he could reach out to them.

The university also set up mobile COVID-19 vaccination clinics at the churches, and church members were encouraged by their pastors to get vaccinated. "If they see someone they know and trust, they follow," Bigham says.

Over time, AMEN has added discussion sessions and classes on topics such as grief, loss, racism, mindfulness and nutrition. Bigham’s church has a community garden where they offer tours to teach visitors about the food they grow and its nutritional value. AMEN aims to “build infrastructure within the church and sustain the program,” Hecht says.

Stephen B. Thomas, director of the Center for Health Equity at the University of Maryland School of Public Health in College Park, founded Health Advocates In-Reach and Research (HAIR). The program focuses on training Black barbers and hairstylists so they can offer customers health education and connect them with medical services. Why barbers? "They have the trust the medical community has lost," says Thomas.

The HAIR program is now up and running in three Maryland counties. One program, supported by a grant from the state of Maryland, involves barbers and hairstylists who provide COVID-19 education and host vaccination events. Thomas received a call from the White House this past year, requesting the HAIR program be part of an initiative to recruit Black barbershops and salons to be part of a national vaccination campaign. The barbers and stylists involved with HAIR also promote and support screenings for colorectal cancer and other conditions. Televisions in the shops feature health programming.

"The message is important, (and) so is the messenger. Trust matters," Thomas says.

Susan Ladika is an independent journalist in Tampa, Florida, who covers healthcare and business.
Can’t sleep as a child? The problem may not go away.

New research finds childhood insomnia often continues into adulthood. by JARED KALTWASSER

For parents, sleep can be a touchy subject. The first few months of parenthood are often marked by incessant, nighttime interruptions of sleep. When the child becomes a teenager, sleep is associated with battles over bedtime and marveling at the teenager’s ability to sleep until noon. However, an increasing amount of evidence is underscoring the role sleep plays in many different areas of health — and childhood sleep is no exception.

In a study recently published in *Pediatrics*, Julio Fernandez-Mendoza, Ph.D., of Pennsylvania State University College of Medicine (Penn State) in Hershey, and colleagues reported that when a child has insomnia symptoms, the most common trajectory is for the sleep problems to persist into adulthood. Approximately 6 in 10 children with insomnia symptoms will either experience persistent symptoms into adulthood or will see a waxing-and-waning pattern, in which the symptoms come and go throughout their lives.

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A previous study suggested nearly half of children with insomnia symptoms see those symptoms remit by early (26.2%) or late (20.9%) adolescence. Findings such as these led to the perception that childhood insomnia symptoms go away as children age. This study finds that is not the case for many children.

"Adolescence is a wonderful stage of life during which a lot is going on psychosocially and biologically. However, it is also a stage of increased vulnerability," Fernandez-Mendoza told *Managed Healthcare Executive*. "Our study showed this from an insomnia perspective, where adolescents with insomnia symptoms who slept shorter in the sleep lab were at a high risk of worsening into an insomnia disorder in young adulthood."

Fernandez-Mendoza and colleagues noted that most of the previous literature was based solely on self- or parent-reports of sleep, rather than objective measures. Most reports also had shorter follow-up periods, with little insight into how patients experienced sleep as adults.

**Longitudinal research**

In this research, investigators used the Penn State Child Cohort, a random, population-based cohort of school-aged children. One thousand members of the initial cohort of more than 5,000 children were asked to undergo in-laboratory polysomnography at the start of the study (between the years 2000 and 2005). Most reports also had shorter follow-up periods, with little insight into how patients experienced sleep as adults.

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NOW APPROVED

Dry eye starts with tear film disruption.¹

Treat by activating tear film production.²

INTRODUCING A WHOLE NEW WAY TO TREAT DRY EYE DISEASE.²

Tyrvaya™, the first and only nasal spray approved to treat the signs and symptoms of dry eye, is believed to activate the trigeminal parasympathetic pathway via the nose, resulting in increased tear film production.² The exact mechanism of action is unknown at this time.

Watch Tyrvaya in action at Tyrvaya-pro.com.

INDICATION

Tyrvaya™ (varenicline solution) Nasal Spray is indicated for the treatment of the signs and symptoms of dry eye disease.

Please see Brief Summary of Prescribing Information on the adjacent page and the full Prescribing Information at Tyrvaya-pro.com.

IMPORTANT SAFETY INFORMATION

Adverse Reactions

The most common adverse reaction reported in 82% of patients was sneezing. Events that were reported in 5-16% of patients were cough, throat irritation, and instillation-site (nose) irritation.

**INDICATIONS AND USAGE**

TYRVAYA™ (varenicline solution) nasal spray is a cholinergic agonist indicated for the treatment of the signs and symptoms of dry eye disease.

**ADVERSE REACTIONS**

**Clinical Trials Experience:** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In three clinical trials of dry eye disease conducted with varenicline solution nasal spray, 349 patients received at least 1 dose of TYRVAYA. The majority of patients had 31 days of treatment exposure, with a maximum exposure of 105 days.

The most common adverse reactions reported in 82% of TYRVAYA treated patients was sneezing. Other common adverse reactions that were reported in >5% of patients include cough (16%), throat irritation (13%), and instillation-site (nose) irritation (8%).

**USE IN SPECIFIC POPULATIONS**

**Pregnancy: Risk Summary:** There are no available data on TYRVAYA use in pregnant women to inform any drug associated risks. In animal reproduction studies, varenicline did not produce malformations at clinically relevant doses.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

**Data: Animal Data:** Pregnant rats and rabbits received varenicline succinate during organogenesis at oral doses up to 15 and 30 mg/kg/day, respectively. While no fetal structural abnormalities occurred in either species, maternal toxicity, characterized by reduced body weight gain, and reduced fetal weights occurred in rabbits at the highest dose (4864 times the MRHD on a mg/m² basis).

In a pre- and postnatal development study, pregnant rats received up to 15 mg/kg/day of oral varenicline succinate from organogenesis through lactation. Maternal toxicity, characterized by a decrease in body weight gain, was observed at 15 mg/kg/day (1216 times the MRHD on a mg/m² basis). Decreased fertility and increased auditory startle response occurred in offspring at the highest maternal dose of 15 mg/kg/day.

**Lactation:** Risk summary: There are no data on the presence of varenicline in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies varenicline was present in milk of lactating rats. However, due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk.

The lack of clinical data during lactation precludes a clear determination of the risk of TYRVAYA to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for TYRVAYA and any potential adverse effects on the breastfed child from TYRVAYA.

**Pediatric Use:** Safety and efficacy of TYRVAYA in pediatric patients have not been established.

**Geriatric Use:** No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.
Can’t sleep as a child? The problem may not go away.

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Adults with insomnia report they had insomnia symptoms as children, and “they never received treatment for them.”

The issue of sleep disorders in childhood also brings up broader questions about the links between sleep and a host of other disorders, which is a question Mendoza-Fernandez and his colleagues are actively studying. After defining the trajectories of childhood insomnia symptoms, “we are now better positioned to relate them to the presence of cardiovascular disorders and mood disorders, such as depression or anxiety disorders, later in young adulthood,” he said. His research team is actively evaluating those data in this cohort, although they are not yet finished.

“Our interim findings indicate that children whose insomnia symptoms persisted over such a long period of time are at increased risk of being diagnosed and treated for a mood or anxiety disorder as young adults. Early prevention will not only help stop the persistence and worsening of insomnia but also potentially prevent adverse mental health outcomes,” he said. Prevention starts by treating sleep problems as an independent condition, rather than simply dismissing it as bad habits or as a symptom of mood or behavior disorders, even if those disorders might contribute to the sleep problem, Mendoza-Fernandez explained.

He also noted cognitive behavioral therapy for insomnia has become a prominent treatment option for adults and can also be applied to adolescents. Fernandez-Mendoza said properly timed bright light therapy is one option to address the body clock issue. He said sleep medications should be seen as a second-line option. Regardless, the results make clear that sleep must be an important part of conversations about the health of children and adolescents. “Evidence shows ... that insomnia in children (requires) specific attention, as it can have a direct impact on daytime behavior — such as social relations or school performance — can be effectively treated and can be diagnosed as a disorder in its own right,” Fernandez-Mendoza said.

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**UNIVERSITY STUDENTS FACE SLEEP, QUALITY-OF-LIFE CHALLENGES AMID THE PANDEMIC**

Few people equate the college years with healthy sleep habits, but a new report finds sleep issues among university students are not only common but also are associated with a lower health-related quality of life (HRQoL). Researchers from Sapienza University of Rome in Italy, noted that in the era of the COVID-19 pandemic, much attention has been paid to how sleep problems caused directly or indirectly by the global health crisis have impacted people’s quality of life. Corresponding author Matteo Carpi, M.S., and colleagues wanted to better understand whether a similar relationship between sleep and quality of life existed among university students.

Carpi and colleagues created an online cross-sectional survey based on four indices of sleep and quality of life. They then administered this survey to Italian university students between March and June 2021. A total of 1,279 students completed the questionnaire, most of whom were women (1,119 respondents). The results, published in the *International Journal of Environmental Research and Public Health*, showed that nearly two-thirds (65%) of respondents reported poor sleep quality and 55% reported symptoms of insomnia. Poor sleep was associated with higher perception of stress and lower physical and mental HRQoL scores.

“Ultimately, our results show a high prevalence of poor sleep among Italian university students during the COVID-19 pandemic and support the relevance of sleep quality for young people’s overall quality of life,” the authors wrote.

They added that the results also highlight the importance of effective interventions and treatment strategies. Carpi and colleagues said cognitive behavioral therapy for insomnia (CBT-I) is an option for many college students.
On Jan. 3, 2022, the federal government officially renewed a declaration that the opioid epidemic is a public health crisis. Although the COVID-19 pandemic has overshadowed the opioid epidemic, the number of people in the U.S. dying from opioid overdoses has recently increased. According to preliminary data from the CDC, the number of overdose deaths from opioids rose to 75,673 in the 12-month period, ending in April 2021, and there was a 35% increase from 56,064 deaths recorded during the prior 12 months.

Federal government agencies and state health officials have taken various steps to clamp down on opioid prescribing in response to the epidemic. For example, most states have set a limit on the amounts of opioids physicians can prescribe. But some oncologists say the well-intentioned efforts have had the unintended consequence of preventing patients with cancer from getting essential pain relief.

“Stricter opioid regulations have not intended for cancer to be the targets, and certainly not [those] who are dying,” she says. Enzinger also found there has been very little research into opioid use among patients with cancer during the opioid epidemic and the crackdown on opioid prescription. She decided to change that.

Enzinger is the lead author of a study on trends in opioid access among patients with cancer who have a poor prognosis that was published last year in the Journal of Clinical Oncology. Enzinger and her team analyzed a data set that included almost 280,000 Medicare beneficiaries with cancer who had a poor prognosis and who died between 2007 and 2017. When they looked at metrics of opioid utilization during the last 30 days of life, they identified a 34% decrease in opioid prescription fills and a 38% decrease in the total dose of opioids filled per decedent.

“That gives a good overall sense of what’s happening. A 38% decline in the amount of opioids prescribed in the last month of life per patient who died is a huge drop, particularly because there is a lot of literature that shows undertreatment of cancer pain has been a major problem,” Enzinger says. “If you are cutting the supply of opioids going to cancer patients, it’s a big problem.”

Enzinger and her colleagues also found a 50% reduction in filled prescriptions for long-acting opioids, which is not surprising, because they’ve been more tightly regulated than short-acting formulations because of their potential for abuse. But Enzinger says patients with severe cancer pain often need long-acting opioids.

“If you have a tumor sitting on your nerve, causing severe pain all the time, (and) if you don’t have a sustained-release medication, you’re chasing your pain all day and have to take something every two hours, even when you are trying to sleep,” Enzinger says. “It’s troubling.”

As opioid prescriptions fell, the results of Enzinger and her colleagues’ study showed that the proportion of patients making pain-related trips to the emergency room decreased.
department increased by 50%. "Among patients with terminal cancer, there have been substantial declines in opioid access and an increase in treatment of pain through the emergency department," Enzinger says. "That suggests strongly that people are not able to manage their pain as well at home or do not have something in their medicine cabinet when having severe pain at night."

**Addiction worries**

As with all medications, opioids have benefits and risks. There is a risk of addiction, particularly for those with a prior history of substance use. Before prescribing, physicians are supposed to assess a person’s addiction risk with a variety of assessment tools. However, the risk of addiction for those with chronic pain and no prior history of substance use is not as common as some might think.

Nora Volkow, director of the National Institute of Drug Abuse, is on record as saying that, unlike tolerance and physical dependence, addiction is not a predictable result of opioid prescribing. "Addiction occurs in only a small percentage of persons who are exposed to opioids, even among those with preexisting vulnerabilities," she said.

A study from the University of Michigan found that approximately 6% of patients who take opioids for the first time to relieve pain after surgery end up taking the medications for longer than clinically recommended. And dependency on opioids is a reality among patients with cancer. A number of studies have shown that because many patients with cancer require opioid analgesia (pain relief) for an extended period, they do, in fact, become dependent on the drug and will need higher and higher doses to get the same pain relief. If they stop taking the drug, they may experience withdrawal symptoms. But dependence and the need for greater doses are secondary concerns if patients are in pain and have a poor prognosis.

Navigating use the appropriate use of opioids is a challenge for patients and physicians, according to experts and countless physicians and patients. Many physicians would like to opioids used for a short while until pain is treated in some other way — with PT, surgery or medications that are less likely to lead to dependency. But often that doesn’t happen. And many see a role for opioids in pain management for patients with cancer even if they are not at the end of life if the drugs help them be comfortable and can help with a good quality of life.

Cindy Steinberg, director of policy and advocacy at the U.S. Pain Foundation, a nonprofit organization sponsored by pharmaceutical companies, says that when pain persists for three months or longer, it becomes a disease of the nervous system and brain. “If it was caused by cancer, it could be from the disease itself damaging nerves or tissue, advanced disease causing increased damage, or the treatment itself, such as the type of chemotherapy or radiation causing damage,” she says.

“The best way to manage any type of chronic pain — including cancer pain — is through an individualized, multidisciplinary approach combining a number of treatment options,” Steinberg says. “There are many different medications that treat pain, and opioids are one important option in the toolbox, particularly for severe pain.”

Enzinger says efforts to combat the opioid epidemic must also balance the needs of patients with cancer who are experiencing pain.

“There is a fear of being addicted or (some patients) think it’s a sign of weakness. Pharmacists asking why they are taking them, which sends the message they shouldn’t be using it. There needs to be more attention that this population needs protecting, even while we as a society are grappling with the opioid epidemic.”

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Reality-checking digital therapeutics as they take off

Digital therapeutics are barreling their way into American healthcare with promises that their special brew of technology, data, convenience and behavior-changing psychology can improve the treatment of many chronic conditions, especially those affecting behavioral health. But digital therapeutics are also stirring up a lot of questions about their limitations, the evidence for their safety and efficacy, and how payers should go about deciding whether they should be covered.

Michael Angelini, Pharm.D., M.A., a professor of pharmacy practice at the Massachusetts College of Pharmacy and Health Sciences University in Boston, and Soumya Vishwanath, Pharm.D., senior manager, formulary management, at Magellan Rx Management in Cambridge, Massachusetts, gave an overview of digital therapeutics and the approaches that payers are taking to them at AMCP 2022.

Angelini provided a brisk survey of the pros and cons of digital therapeutics for behavioral health. Vishwanath presented research on some of the approaches that payers are taking to them at AMCP 2022.

Vishwanath also noted that 68% of digital therapeutics currently in development (“in the pipeline”) are for psychiatric and neurologic conditions. Data she shared showed a tally of 23 digital therapeutics for behavioral health being currently available, 10 in a pivotal trial, and 46 in early-phase, proof-of-concept research. By Vishwanath’s count, a total of 137 digital therapeutic products for behavioral health are in the pipeline.

Drug launches, pandemic COVID-19 and more reshape U.S. health care in 2021-2022

The COVID-19 pandemic has scrambled many sectors of the American economy and life the past two years, including delivery of healthcare services and some aspects of the pharmaceutical industry. In a keynote address, Doug Long, MBA, vice president of industry relations at IQVIA, described some of the disruptions, sketched the trends and made projections about the near-term future of U.S. healthcare.
Overall, Long gave the “health ecosystem” an A+ for its response to the pandemic, pointing to the success of bringing three vaccines to market in record time, scaling up vaccine production and adjusting the supply chain processes to handle volume increases and decreases.

“So, an A rating and congratulations,” said Long, a seasoned presenter at healthcare meetings. He compared the healthcare sector to the automobile industry: “Think about how this ecosystem held up better than trying to get a car today,” he said.

Long also gave an overview of the pharmaceutical market. The growth in the specialty market continues to outpace the growth of traditional drugs; however, conventional wisdom had expected specialty to have been larger than traditional at this point. Although that hasn’t happened yet, Long expects it to do so in 2022. Right now, traditional drugs account for 50.3% of the total nondiscounted spend compared with 49.3% for specialty.

Generic sales continued to decline and were down 5.2% in January 2022 because of price deflation, said Long, who also projected cost savings coming from biosimilars: “We’re in the sweet spot of biosimilars now.” He said that between 2020 and 2024 the savings from biosimilars prescriptions should reach $104 billion.

**Prevalence of alopecia areata is increasing**

Research presented at AMCP’s annual meeting suggests that the prevalence of alopecia areata is increasing among those with employer-sponsored health insurance. Markqyne Ray, Pharm.D., MBA, of Pfizer and colleagues used the IBM MarketScan database to identify claims related to alopecia areata, an autoimmune disorder characterized by hair loss. The condition has become well known lately because of Will Smith’s slapping of Chris Rock during the Oscars ceremony after Rock made a joke about Smith’s wife’s shaved head. Jada Pinkett Smith cut her hair because she has alopecia.

After applying some statistical adjustments, they found that claims submitted suggest that prevalence (the number of existing cases) of alopecia areata had crept steadily upward between 2016 and 2019, from 0.199% in 2016 to 0.212% in 2017, to 0.219% in 2018 and to 0.222% in 2019. Their calculations also show prevalence is about 60% higher among females (0.252%-0.271%) than among males (0.145%-0.171%) and higher among adults (0.220%-0.245%) than among children (0.120%-0.135%).

Ray and colleagues also calculated the incidence (new cases) by identifying a claim for medical service related to alopecia areata with no diagnosis the year before. The trend in incidence was not as clear as the one in prevalence. According to the research reported at AMCP 2022, the incidence was 91.46 per 100,000 person-years in 2016, 87.39 in 2017, 91.32 in 2018 and 92.9 in 2019. As with prevalence, incidence was quite a bit higher among females than among males (0.252%-0.271%) than among males (0.145%-0.171%) and higher among adults (0.220%-0.245%) than among children (0.120%-0.135%).

**Atopic dermatitis treatment is in a good place, but...**

Newly approved medications. Others in the offing that are in late-stage clinical trials. Peter Lio, M.D., said clinicians and patients are now experiencing one of the brighter chapters in the history of treatment of atopic dermatitis.

“The biggest difference is just the awareness,” said Lio, a clinical assistant professor of dermatology and pediatrics at Northwestern University Feinberg School of Medicine and founding director of the Chicago Integrative Eczema Center. “That is one of those unintended consequences of (pharmaceutical) companies actually focusing on it. People are talking about it. They are preparing to get better for the first time. They are coming back to our clinic.”

Lio, who specializes in patients with severe atopic dermatitis, was one of the speakers at a satellite symposium on atopic dermatitis at AMCP 2022. He credited Dupixent (dupilumab), an injectable biologic approved in 2017, with ushering in a new era for atopic dermatitis treatment. “It has changed everything and allows us to really offer sustained control for a huge group of people who never had it before, in a really safe way,” he said.

In a brief interview after his presentation, Lio also discussed problems that clinicians and patients are facing, one of the main ones being step therapy. “The idea of (step therapy) makes sense and is reasonable. You don’t want people starting on a super-powerful medicine,” Lio said. “It is just in the details that it is incredibly challenging, and the more complex patients are, the more severe their disease, the worse it is.” Another panelist, Neil Minkoff, M.D., chief medical officer for Coeus Consulting, shared the results of a survey of patients with atopic dermatitis that showed 50% had experienced a delay or denial of prescription in the past 12 months. The survey also showed that half of the denials were due to step therapy and 60% of the delays were due to prior authorization.
Michael Zeglinski, senior vice president and CEO of Optum Specialty and Infusion pharmacies, shared data showing that 42% of atopic dermatitis patients have out-of-pocket expenses of $1,000 or more and 8.5% reported costs of more than $5,000. High out-of-pocket costs are linked to nonadherence among patients taking oral cancer drugs

Oral cancer treatments are becoming increasingly common and have many advantages, especially the convenience of “popping a pill” at home. Even so, research presented at AMCP 2022 showed that almost half of patients on oral cancer treatments are nonadherent. For many types of cancer, high out-of-pocket costs and low income contributed to the patients not taking the medication as prescribed, the research showed.

Ami Vyas, Ph.D., M.S., MBA, an assistant professor of pharmacy practice at the University of Rhode Island College of Pharmacy, and her colleagues found that almost half (48.1%) of the nearly 38,000 patients with cancer in their study were nonadherent to oral cancer treatments. Vyas explained in an email that injectable therapies are generally covered under medical benefits in people’s insurance plans, whereas oral drugs are covered through prescription drug plans that may charge coinsurance (a percentage of the drug’s price, so if the drug is expensive, the out-of-pocket expense is high).

“A very limited number of oral anti-cancer medications have injectable equivalents, and most of the newer oral anti-cancer medications don’t have any,” Vyas said in the email. “If there is no alternative to oral medications, then it leaves patients with no choice but to fill the expensive oral medications or abandon the prescription if they cannot afford it.”

Vyas and her colleagues used the de-identified Optum Clininformatics Data Mart commercial claims database for 2010-2018 to conduct their research.

The proportion of adherence varied with the type of cancer, according to their findings. Adherence was lowest for patients with liver cancer; just 32.8% were adherent. It was highest (70.4%) for patients with brain tumors. Vyas and her co-researchers also found large differences in the monthly out-of-pocket costs by the type of cancer. Patients with blood cancer had the highest monthly out-of-pocket cost, $749.

RWE research keeps coming on strong, says journal editor-in-chief

More research yielding real-world evidence (RWE) and an uptick in studies evaluating health disparities and social determinants of health are among the trends seen by Laura E. Happe, Pharm.D., M.P.H., in the research presented AMCP annual meeting this year.

Happe is editor-in-chief of the Journal of Managed Care & Specialty Pharmacy, which is published by AMCP. Outside reviewers and other editors at the journal rate the abstracts of the research that is submitted for presentation at the meeting. Happe, who has been editor-in-chief of the journal for a little more than nine years, reviews and finalizes the ratings and the acceptance decisions. “We saw a lot of RWE studies in therapeutic areas with new drugs or indications approved in the past few years, such as oncology and autoimmune disorders, as the real-world data for these products are maturing,” Happe said. The number of submissions increased during the COVID-19 pandemic, noted Happe. “Now that business is beginning to return to normal,” she said, “submissions are leveling out to pre-pandemic levels.

More than 100 pharmacy students presented research at this year’s meeting, according to Happe, and a large proportion of their research focused on the effects of direct patient care services or benefit design on patient outcomes.