RADAR on Specialty Pharmacy

Strategies and Analysis for Managing High-Cost Specialty Products

March 2021

VOLUME 18 | NUMBER 3

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FDA Approval Makes Breyanzi Third CAR-T Therapy in NHL

With the FDA's approval of Bristol Myers Squibb's (BMS) Breyanzi (lisocabtagene maraleucel) last month, there are now three chimeric antigen receptor T cell (CAR-T) therapies to treat a certain type of non-Hodgkin's lymphoma (NHL). A Zitter Insights poll shows that payers do not anticipate its approval as having much of an impact on their management of the space. However, with more of these therapies in the pipeline, payers should take a closer look at these therapies and their management of them, say industry experts.

On Feb. 5, the FDA approved Breyanzi for the treatment of adults with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma not otherwise specified, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma and follicular lymphoma grade 3B (see brief, p. 8). The agency gave the CD19-directed CAR-T therapy orphan drug, regenerative medicine advanced therapy and breakthrough therapy designations.

CAR-Ts are one-time treatments that consist of extracting a person's white blood cells, reprogramming them to recognize and attack the cancer cells and then reinfusing them into the patient. As of early March, Breyanzi's website listed 23 authorized treatment centers across the U.S. BMS plans to manufacture Breyanzi at its Bothell, Wash., facility.

continued on p. 10

CVS-CTCA Pilot Offers In-Home Infusion of Cancer Therapies

As the U.S. surpasses 500,000 deaths from the COVID-19 pandemic, people with cancer continue to unsurprisingly be hesitant to visit a provider office or hospital for treatment. So, Cancer Treatment Centers of America (CTCA) is working with CVS Health to bring therapies into certain patients' homes, helping keep immunocompromised people safer and allowing them to continue much-needed cancer treatment.

Multiple studies have shown how the pandemic has affected all aspects of cancer care, from screening and diagnostic workups to actual oncology treatments, follow-up services and patient support *(RSP 6/20, p. 1)*. "The COVID-19 pandemic created new challenges for immunocompromised patients with cancer looking for ways to safely continue their care while minimizing their exposure to the virus," explains Sree Chaguturu, M.D., senior vice president at CVS Health and chief medical officer at CVS Caremark. "CTCA is seeing a 50% reduction in infusions, and, while a slight delay in treatments may have been appropriate at the pandemic's onset, data is now pointing to increased mortality risk with every month of delayed care. There is a critical need for providing in-home therapy where possible to safely treat patients who are immunocompromised."

Published by AIS Health, Washington, DC. An independent publication not affiliated with insurers, vendors, manufacturers or associations.

To meet that need, CVS and CTCA — a national oncology network of hospitals and outpatient care centers — recently launched a pilot program known as Oncology Clinic at Home to boost access to in-home chemotherapy for patients meeting certain criteria. The offering is one of a growing number of telehealth services offered by CTCA Anywhere, CTCA's virtual visit technology.

To qualify, patients must:

✦ ***Be in good health and demonstrate they can tolerate their therapies in an inpatient setting;***

✦ ***Be undergoing treatment with certain types of chemotherapies or immunotherapies;***

✦ ***Live in a state allowing in-home infused cancer treatments;***

✦ ***Have reliable internet service;***

✦ ***Own and be comfortable using a laptop, computer, smartphone or tablet***; and

✦ ***Have in-home infusion covered by their health insurance policy.***

CTCA says that the drugs qualified to be in-home administered are for "many of the most common cancers," including breast, colorectal, head and neck, lung and prostate cancers, as well as some genitourinary cancers. CVS ships the therapies, as well as any equipment needed to administer them and to monitor patients' progress, directly to patients, who also are given instructions on handling them.

The pilot launched in the Atlanta area only, but there are plans to expand it. CTCA Atlanta "is located in Newnan, Ga., and recently received Magnet designation by the American Nurses Credentialing Center (ANCC), the highest national honor for nursing excellence. At CTCA Atlanta's Lung, GI and Breast Cancer Centers, experienced cancer experts and multidisciplinary teams are committed to delivering comprehensive, integrated care, all in one location. With one of the largest patient bases in the CTCA national oncology network and given the unique rural health care needs of the Georgia patient population, CTCA Atlanta made sense as the pilot location."

CVS provides the service via its Coram specialty infusion services subsidiary. "By combining home infusions performed by chemotherapy-trained nurses with telehealth oversight and a proprietary technology platform (including patient-reported outcomes and remote patient monitoring), we provide consistent connectivity between the CTCA provider and in-home care team," explains Chaguturu. "This ensures the highest levels of safety."

Coram provides infusion therapy services to more than 205,000 people annually in both outpatient and home-based settings, he says. The company offers services at more than 90 locations across the U.S., including more than 70 ambulatory infusion suites, and it has the ability to reach 97% of the U.S. population. "Through Coram, CVS is able to meet people wherever they are and change health care to meet their needs," Chaguturu says. "Given our commitment to offering diversified health services, we foresee more opportunities to deliver home-based care plans for patients being treated for chronic illnesses."

Nurses Have Oncology-Specific Training

Coram nurses have training in chemotherapy administration based on Oncology Nursing Society guidelines, "which focus on safety concerns related to environment of care; treatment planning and patient education; ordering, preparing, dispensing and administering chemotherapy; and monitoring for toxicities, adherence and complications following administration," he tells AIS Health. "In addition to this,

RADAR on Specialty Pharmacy (ISSN: 2576-4438) is published 12 times a year by AIS Health, 2101 L Street, NW, Suite 300, Washington, D.C. 20037, 800-521-4323, www.AISHealth.com.

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Coram nurses receive training from CTCA both in didactic and on-site forums."

The care providers are compliant with infection protocols and proactive prevention techniques that are aligned with guidance from the Centers for Disease Control and Prevention aimed at minimizing exposure to and community-based transmission of COVID-19. In addition, the company contacts patients before going into their homes "to understand potential COVID-19 infection or exposure and to ensure continued safety for our clinicians and our patients."

Patient Care Teams Are Available 24/7

"A patient's care team is available around the clock to answer questions and provide the support patients need," he says. "Once home, patients will receive in-home Coram nurse visits to administer the therapy, paired with regular telehealth visits and digital therapeutic check-ins with their CTCA clinician, care team, pharmacists and other clinical staff as needed."

"The pandemic has created added challenges for immunocompromised patients who need cancer care, a major pain point this pilot is aiming to address," states Chaguturu. "Even in normal times, CTCA understands the challenges many patients endure to receive chemotherapy — whether they live down the street or hundreds of miles from their hospitals. CTCA strives to make chemotherapy infusions and injections as comfortable and convenient as possible — including by giving qualifying patients the option of receiving these treatments at home. The scope of this program will be determined by the demand for at-home oncology services and the success of the pilot in meeting those needs."

Ultimately, he says, "We're proud of the way that we have responded and adapted to new demands during this public health crisis. We will continue to look for ways to meet patients where they are, and help them get the care they need, when and where they need it."

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New Long-Acting HIV Regimen May Help Patient Adherence

The FDA recently approved the first long-acting regimen for the treatment of HIV in adults. The dosing schedule could help with adherence in a condition where that is particularly crucial. However, some potential challenges exist with the medication, including whether health plans actually will cover it.

On Jan. 21, the FDA approved ViiV Healthcare's Cabenuva (cabotegravir and rilpivirine) for the treatment of HIV-1 infection in adults to replace a current antiretroviral regimen in people who are virologically suppressed on it with no history of treatment failure and no known or suspected resistance to either cabotegravir or rilpivirine.

The agency also approved the tablet Vocabria (cabotegravir) to be taken with Johnson & Johnson unit Janssen Therapeutics' tablet Edurant (rilpivirine) for one month before starting treatment with Cabenuva to ensure the medications are well-tolerated before switching to the extended-release injectable formulation. Cabenuva is the first and only complete long-acting regimen for the treatment of HIV-1 in adults.

Dosing is via two separate single-dose vials, one of cabotegravir and one of rilpivirine. The recommended starting dose is Cabenuva 600 mg/900 mg on the last day of the oral lead-in regimen and then Cabenuva 400 mg/600 mg each subsequent month. Dosing of the intramuscular injectables must be done by a health care professional. Pricing of the initial dose is $5,940, and subsequent monthly doses will be $3,960. According to STAT News, the company is providing the 30-day lead-in regimen at no charge to patients.

"Today's FDA approval of Cabenuva represents a shift in the way HIV is treated, offering people living with HIV a completely new approach to care," said Lynn Baxter, head of North America for ViiV Healthcare, in a press release. "Cabenuva reduces the treatment dosing days from 365 days to 12 days per year. At ViiV Healthcare, we are dedicated to ensuring no one living with HIV is left behind, and adding this first-of-its-kind regimen to our industry-leading portfolio of innovative medicines reinforces our mission."

Company Was Formed to Focus on HIV

ViiV is majority owned by GlaxoSmithKline plc, with Pfizer Inc. and Shionogi Limited as shareholders. It was established in November 2009 to focus specifically on the treatment and care of people with HIV and people at risk of becoming infected with it.

"The approval of Cabenuva allows some HIV-1 infected patients the option of receiving a once-monthly injection instead of a daily oral treatment regimen," points out Nicole Kjesbo, Pharm.D., clinical program development director at Prime Therapeutics LLC. She tells AIS Health that the drug is "a good option for patients that are nonadherent to an everyday regimen."

According to ViiV, in clinical trials, nine out of 10 patients preferred Cabenuva over their previous daily oral therapy. In a Jan. 26 Anton Rx Report, executive editor Bill Sullivan wrote that in Europe, where the drug became available last year, "patient feedback has been surprisingly popular in spite of the fact that the therapy requires an office visit for the monthly injections. A patient survey in Europe showed that two-thirds of HIV patients were 'likely' to switch to a long-acting injectable regimen."

Drug Offers 'Greater Freedom'

In a statement, Brett Andrews, CEO of PRC, a San Francisco-based organization that offers services to people with HIV/AIDS, substance use or mental health issues, said that "for years, many of our clients have struggled to manage their health while working to stabilize key aspects of their lives. Cabenuva will provide some people living with HIV greater freedom to pursue vocational, educational and other opportunities, like travel, without the need for daily oral medication management. A long-acting regimen is an innovation we have been waiting for."

Early HIV treatment regimens consisted of a variety of pills, but many medications are now available as a once-daily agent. "In recent years, the burden associated with HIV regimens has become less," observes Kjesbo. "Instead of taking multiple drugs and doses multiple times a day, there are now options to take one combination pill orally once a day." With these treatments, "adherence is essential. HIV medications taken every day prevent HIV from multiplying and reduce the rate of resistance. Nonadherence can lead to drug resistance and HIV treatment failure."

In addition to reduced pill burden, Sullivan wrote that another benefit of Cabenuva addresses the fact that "HIV patients are concerned with their privacy. A once a month office injection eliminates having lots of HIV pills in the medicine cabinet." He also pointed out that people with HIV may visit a clinician approximately every three to six months, so "seeing a clinician monthly facilitates virus level monitoring, promotes disease education, nutrition and psychological counseling, and identification of emergent concomitant medical issues."

The drug will be available both via specialty pharmacy and buy and bill. ViiV has selected 14 specialty pharmacies to be in its network; for providers buying and billing Cabenuva, there are six specialty distributors available.

Physicians Are Likely to Prescribe It

In a Zitter Insights survey of 50 physicians conducted between Aug. 30, 2019, and Oct. 2, 2019, 68% of respondents said they were likely to prescribe Cabenuva for patients with a history of adherence issues. Its route of administration and dosing regimen were the main factors influencing their expected prescribing of it. And among 51 commercial payers with 162.7 million covered lives, 39% said they expected to manage the drug at parity with certain HIV therapies.

However, challenges could exist around people's unwillingness to get an injectable medication, Kjesbo says, noting that "injection site reactions occurred in 83% of patients treated with Cabenuva, including 37 with at least a Grade 2 (moderate) reaction."

According to Kjesbo, "The patient population who will elect to take this will be those that agree to visit their health care professional once per month.…Adherence is crucial with a once-monthly injection. If a patient plans to miss a scheduled injection visit by more than seven days, they will have to take daily oral therapy to replace up to two consecutive monthly injection visits. In addition, if monthly injections are missed or delayed by more than seven days and oral therapy has not been taken in the interim, the patient will have to be reassessed to determine if resumption of injection dosing remains appropriate."

At Prime, she says, "we anticipate that most health plans will cover the drug in some capacity. Some states also have legislation around HIV requiring coverage."

Drug Will Fall Under Medical Benefit

Because the drug is administered by a health care professional, "it will largely be adjudicated on the medical benefit and managed through medical policy," she explains. "Plans may choose not to create a medical policy given this population is generally managed by an HIV specialist. If a plan chooses to manage this drug, potential criteria may include verification the patient has initiated therapy with the oral regimen required and has active HIV infection (to ensure it is not used off-label for HIV prophylaxis). In addition, they may apply a dose check to ensure appropriate dosing and/or documentation of adherence to the regimen."

The FDA approval comes a little bit more than a year after the FDA issued a complete response letter for the drug in December 2019, citing manufacturing concerns. According to an Endpoints News article, Kimberly Smith, ViiV's head of research and development, said "that delay was 'obviously disappointing,' but was — in hindsight — a blessing as it allowed the drugmaker to add even more

long-term safety data to its reworked application." She told the outlet that the company "worked very closely with our colleagues in CMC [i.e., the FDA's Chemistry, Manufacturing, and Controls] to make sure we clarified to the FDA…what the questions were and how we addressed them. It was particularly important for us to make sure that we nailed it."

And while launching a drug that needs to be professionally administered during a pandemic might seem challenging, Endpoints News also reported that "some clinics have established special lines for patients to receive their injections during Covid-19 and others had created designated parking spaces for patients to get the shots without entering the building."

ViiV Is Applying for Use Every Two Months

On Feb. 24, ViiV submitted a supplemental New Drug Application to the FDA for Cabenuva use every two months. A clinical trial showed that dosing was noninferior compared with once-monthly administration. "A big problem with HIV therapy has been missed doses, very often due to loss of insurance coverage," wrote Sullivan. "A two-month, long-acting injectable regimen would help bridge coverage gaps."

The company also is studying injectable cabotegravir as a pre-exposure prophylaxis (PrEP) treatment. On Nov. 9, 2020, ViiV said an independent data safety monitoring board recommended early unblinding of a study evaluating the safety and efficacy of the drug for HIV prevention in women after the study showed that cabotegravir was 89% more effective than daily oral emtricitabine 200 mg/tenofovir disoproxil fumarate 300 mg, available as Gilead Sciences, Inc.'s Truvada. Earlier last year, another study showed injectable cabotegravir was 69% more effective than Truvada in preventing HIV acquisition in men who have sex with men and transgender women who have sex with men.

However, in July 2020, Arafa Salam, Ph.D., an infectious diseases analyst at GlobalData, wrote that Truvada — for which a generic version is now available — may remain the preferred PrEP treatment due to Cabenuva's cost and potential adherence issues.

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Evolution of Medicine Has Produced Novel New Treatments

Therapeutic interventions have evolved from people taking a pill every day to treat a condition to the one-time cell and gene therapies aimed at halting disease progression or even curing a disease. The rise of these innovative new products means that payers need more information than ever in order to properly assess treatments, as well as updated reimbursement models.

"The science is moving at lightning speed, and what we thought was previously impossible has now become a reality with some of the newer gene therapies and other novel drug approvals," observes Reta Mourad, Pharm.D., a senior director on the access experience team at PRECISIONvalue. "As we learn more about diseases and develop a deeper understanding down to the genetic and molecular level, we are able to see advances in therapies that were unheard of," for example with chimeric antigen receptor T cell (CAR-T) therapies, the first of which were approved in 2017.

"Medicine today has evolved by leaps and bounds from what it was even a few decades ago. Starting off with small molecule drugs and vaccines, to biologics such as antibody treatments, the world has now evolved into complex therapeutic interventions whereby the genetic construct of an individual patient or the patient's disease is being targeted to cure the disease," point out Amit Agarwal and Brian Corvino, both managing directors at Deloitte Consulting LLP. "The world has moved from treating large homogenous populations where one would treat symptoms to triaging treatments based on the heterogeneity of populations."

Jeff Stoll, KPMG's U.S. life sciences strategy leader, notes that the drug pipeline is filling up with cell and gene therapies. "As of January 2020, 900 different gene therapy IND [i.e., Investigational New Drug] applications were submitted to the FDA, and the market is expected to grow to $62 billion by 2026. These therapies are a key part of the future of pharma.

"The potential to cure or create a functional cure of a disease is slowly becoming a real possibility with these new treatment modalities coming from cell and gene therapies," he continues. "It will take time, but today many monogenic diseases have the potential to be cured through gene therapy. It is this promise that has motivated the pharmaceutical industry to invest heavily into these emerging areas."

New Payment Models Are Needed

But while payers may have standard metrics to conduct value assessments, Agarwal and Corvino contend that the reimbursement models in use today "are antiquated and have not evolved as rapidly as the pace of scientific innovation. Many medicines today have advanced to models such as one-time cures or controlled disease man-

agement. As such, payers have been exploring a range of payment models based on the value imparted by these. Value assessment in itself is very different from financing for these diseases. Defining value entails quantifiable metrics such as financial-risk-based metrics and outcomes-based. However,…the measurement of value offered by treatments, in terms of slowing disease progression vs. curing the disease is yet to be determined."

"Payers will always view a treatment from the lens of total cost of care," maintains Mourad. "Does this therapy that either slows disease progression, halts progression or cures the disease ultimately lower the payer's total cost of care? Does it provide patients with an option that doesn't currently exist in the market? There has to be inherent value in a payer making the decision to pay for a treatment due to the sheer cost of many of these new drug therapies. If a drug is curative but costs upwards of hundreds of thousands of dollars, a payer will need to ensure that the data presented support their decisions as well as understand the potential cost mitigation that may occur by covering the drug vs. the cost of treatment and other medical expenses if the disease is not cured."

Drugs Pose Opportunities, Challenges

New drugs that could be curative, particularly in rare diseases, oncology and other high-cost categories, "pose both opportunities and challenges" for payers, she tells AIS Health. On the one hand, they present new treatment options to patients "and could potentially offset extremely high, ongoing direct and indirect medical costs of treating these diseases with conventional or current therapy." In addition to improved patient outcomes, say Agarwal and Corvino, these agents could "reduce wastage of drug products, minimize unnecessary medical procedures and treatment, and, therefore, decrease cost to members and payers."

However, says Mourad, challenges exist around "being able to support coverage based on the available evidence. Many payers no longer rely just on FDA approval of a therapy as grounds for coverage and will look to guidelines from organizations such as the NCCN [i.e., National Comprehensive Cancer Network] and ICER [i.e. Institute for Clinical and Economic Review], as well as supplemental literature, in order to be able to make more thorough and holistic coverage decisions."

Payers Often Make Coverage Changes

As payers conduct close analyses of these therapies, they are "looking for more than just pivotal trials in order to allow access" says Mourad. "In addition, gone are the days when a coverage decision is made and is essentially permanent. These days, payers are looking for long-term data in order to maintain their existing policies and will often make changes to these policies in light of newly available data. Finding ways to collaborate with payers and other stakeholders is essential for manufacturers to assess early on in the development and study of their therapies."

Drugmakers also can offer more innovative contracts, such as rebate-based agreements, advise Agarwal and Corvino. Or they could "price more effectively or establish certain value-based contracting models," such as "only allowing payments by payers in cases where the product works or reimbursement [is] only for a defined population or different contracts for differential populations. Contracting, thus, can also be a mechanism that allows one to overcome budgeting limitations."

They note that, particularly for high-cost innovative drugs whose value may be delayed, some "innovative coverage models" already are in use. "One popular model is the 'outcome-based + rebate model,' where a payer pays directly for the drug but receives refunds/rebates if the treatment is ineffective or wears off before a certain period of time. The other model is 'outcomes-based + mortgage payments,' where the payer makes a fixed upfront payment and then makes a few additional payments in installments at specified time periods based on the progression or regression of the disease. Other unique models have been built in close collaboration with the federal government for certain essential benefits (such as the COVID-19 vaccine). Additionally, payers have launched programs for rare gene therapies as an additional coverage that patients and employers can buy."

Medicine Will Be 'Hyper-Personalized'

As medicine continues to evolve, what can we expect to see?

Agarwal and Corvino say multiple trends are anticipated. "Precision medicine, for one, is predicted to become hyper-personalized, whereby you are developing a treatment for a disease, especially rare diseases, specifically tailored to an individual patient, rather than a host of patients with the same disease. Secondly, we can expect to see the use of technology, including wearables and real-world data, in helping monitor patients remotely and better predict outcomes. Lastly, getting a holistic picture of every patient's health by including omics data, be it genomics, proteomics or metabolics, as well as environmental information, will lead to better customization of medicines."

According to Stoll, "the knowledge being gained from genetics, biomarkers and in engineering is being deployed to improving medical care. We're at a unique point in the innovation curve when it comes to using genetics to help personalize care. We've seen the cost of genetic screening fall to a point where people are paying for tests for less than $100, compared to the mapping of the genome project that cost billions of dollars 20 years ago. This might not translate immediately, but it lowers hurdles to build upon the work. A bigger question is whether genetics will take health care in the same pattern of lower costs that we've seen in computing, which an entire room of computing power in the 1960s is now capable of being contained in a phone at a fraction of the cost."

In addition, he says, "the next 10 years will see the medical profession expand toward greater expertise around genetics and the ability to understand the role of nucleic acid-based thera-

Biosimilar Uptake Is More Related to Practice Setting Than Patient, Physician Characteristics

by Jinghong Chen

Practice setting and hospital outpatient ownership status had the strongest associations with the adoption of the first three biosimilars launched in Medicare, according to a recent study published in JAMA Network Open. By analyzing use of the biosimilar versions of filgrastim and infliximab among more than 40,000 Medicare fee-for-service beneficiaries, the study found that patient and physician characteristics did not strongly correlate with whether a patient received a biosimilar. While the setting of administration had the greatest association with biosimilar uptake, the direction of association differed by drug class. For instance, a patient in a hospital outpatient setting was 16 percentage points less likely to receive a filgrastim biosimilar than a patient in an office setting, but 3 percentage points more likely to receive an infliximab biosimilar.

Patients Who Received a Biologic by Receipt of at Least One Filgrastim Biosimilar Administration

Patient Characteristic	Absolute Difference Between Patients Received at Least One Biosimilar & Who Never Did (Filgrastim Sample (Q3 2015-Q4 2018))
Age	
65-74	-2.8%
≥75	2.9%
Relevant Medical Conditions	
Acute Myeloid Leukemia	0.6%
Bone Marrow Harvest	0.1%
Bone Marrow Transplantation	-1.0%
Neutropenia	-3.2%
Nonmyeloid Malignant Neoplasm	1.0%

Physicians Who Administer Biologics by Filgrastim Biosimilar Administration

Physician Characteristic	Absolute Difference Between Physicians Administered at Least One Biosimilar & Who Never Did (Filgrastim Sample (Q3 2015-Q4 2018))
Specialty	
Hematologist-Oncologist	5.1%
Oncologist	-0.1%
Other Cancer-Related	0.8%
Primary Care	-1.8%
Other	-4.0%
Volume of Biologic	
Low-Volume Prescriber	-12.4%
Medium-Volume Prescriber	6.6%
High-Volume Prescriber	5.8%

Association Between Filgrastim Biosimilar Administration & Practice Characteristics

Practice Characteristic	Adjusted Biosimilar Rate
Practice Setting	
Office	38.1%
Hospital Outpatient Department	22.0%
Office Practice Characteristic: Office Size	
< 5 Physicians	31.9%
6-19 Physicians	41.4%
20-100 Physicians	43.8%
≥100 Physicians	35.9%
HOPD Practice Characteristic: Hospital Ownership	
Nonprofit	22.0%
For-Profit	4.6%
Government	25.0%

Patients Who Received a Biologic by Receipt of at Least One Infliximab Biosimilar Administration

Patient Characteristic	Absolute Difference Between Patients Received at Least One Biosimilar & Who Never Did (Infliximab Sample (Q4 2016-Q4 2018))
Age	
65-74	-1.1%
≥75	1.0%
Relevant Medical Conditions	
Ankylosing Spondylitis	-0.9%
Crohn Disease	-3.3%
Plague Psoriasis	1.6%
Psoriatic Arthritis	1.6%
Rheumatoid Arthritis	3.5%
Ulcerative Colitis	-2.2%

Physicians Who Administer Biologics by Infliximab Biosimilar Administration

Physician Characteristic	Absolute Difference Between Physicians Administered at Least One Biosimilar & Who Never Did (Infliximab Sample (Q4 2016-Q3 2018))
Specialty	
Dermatologist	0.1%
Gastroenterologist	-2.1%
Rheumatologist	13.6%
Primary Care	-13.0%
Other	1.4%
Volume of Biologic	
Low-Volume Prescriber	-17.7%
Medium-Volume Prescriber	3.4%
High-Volume Prescriber	14.3%

Association Between Infliximab Biosimilar Administration & Practice Characteristics

Practice Characteristic	Adjusted Biosimilar Rate
Practice Setting	
Office	4.1%
Hospital Outpatient Department	7.0%
Office Practice Characteristic: Office Size	
< 5 Physicians	4.3%
6-19 Physicians	2.5%
20-100 Physicians	6.9%
≥100 Physicians	3.3%
HOPD Practice Characteristic: Hospital Ownership	
Nonprofit	6.3%
For-Profit	17.0%
Government	6.1%

SOURCE: "Physician, Practice, and Patient Characteristics Associated With Biosimilar Use in Medicare Recipients," JAMA Network Open. 2021;4(1):e2034776.

peutics (e.g. mRNA, gene therapy and modified cell therapies)."

"Payers are attentive to therapeutic areas that in the past have been treated with more traditional oral therapies and are now advancing into more specialty and medical benefit treatments, such as injections and infusions," explains Mourad.

"These garner increased reviews, as payers need to weigh the benefits of more complex and costly therapies compared with existing treatments. The future of medicine is promising and continues to be a whirlwind," she continues. "COVID-19 has dominated the headlines currently, and that will continue for some time. Gene and cell therapy, as well as genome editing, will advance and garner much attention. The oncology pipeline has and will

New FDA Specialty Approvals

- ***Feb. 3: The FDA gave accelerated approval to Merck KGaA unit EMD Serono, Inc.'s Tepmetko*** (tepotinib) for the treatment of adults with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations. The agency gave the drug priority review and breakthrough therapy and orphan drug designations. The therapy was approved under the FDA's Real-Time Oncology Review pilot program. Dosing for the tablet is 450 mg via two 225 mg tablets once daily. The list price of a 30-day supply is $20,898. Visit www.tepmetko.com.

- ***Feb. 5: The FDA approved Bristol Myers Squibb's Breyanzi*** (lisocabtagene maraleucel) for the treatment of adults with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma not otherwise specified, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma and follicular lymphoma grade 3B. The agency gave the CD19-directed chimeric antigen receptor T cell (CAR-T) therapy orphan drug, regenerative medicine advanced therapy and breakthrough therapy designations. The list price for the one-time treatment is $410,300. Visit www.breyanzi.com.

- ***Feb. 5: The FDA granted accelerated approval to TG Therapeutics, Inc.'s Ukoniq*** (umbralisib) for two indications: for the treatment of adults with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20 based regimen and for the treatment of adults with relapsed or refractory follicular lymphoma who have received at least three lines of systemic therapy. The drug is the first and only oral inhibitor of phosphoinositide 3 kinase (PI3K) delta and casein kinase 1 (CK1) epsilon, according to the company. The agency gave the MZL indication breakthrough therapy designation; both indications had orphan drug designation. Dosing is 800 mg via four 200 mg tablets once daily. The wholesale acquisition cost for a 30-day supply is $15,900. Visit https://ukoniq.com.

- ***Feb. 9: The FDA expanded the label of Regeneron Pharmaceuticals, Inc. and Sanofi Genzyme's Libtayo*** (cemiplimab-rwlc) to treat people with advanced basal cell carcinoma (BCC) previously treated with a hedgehog pathway inhibitor or for whom an HHI is not appropriate. The agency gave the drug full approval for people with locally advanced BCC and accelerated approval for people with metastatic BCC. The FDA initially approved the drug on Sept. 28, 2018 *(RSP 10/18, p. 8)*. It gave the newest use priority review. Recommended dosing for the programmed death receptor-1 (PD-1) inhibitor is 350 mg as a 30-minute intravenous infusion every three weeks. Website Drugs.com lists the price of a 350 mg/7 mL vial as more than $9,652. Visit www.libtayo.com.

- ***Feb. 11: The FDA approved Regeneron's Evkeeza*** (evinacumab-dgnb) as an adjunct to other low-density lipoprotein cholesterol-lowering therapies to treat people at least 12 years old with homozygous familial hypercholesterolemia. It is the first FDA-approved therapy that binds to and blocks the function of the protein angiopoietin-like 3 (ANGPTL3). The agency gave the drug priority review, as well as orphan drug and breakthrough therapy designations. The recommended dose is 15 mg/kg once monthly by a 60-minute intravenous infusion. Dosing is weight-based, and Regeneron says the average annual wholesale acquisition cost is expected to be approximately $450,000. Visit https://evkeeza.com.

- ***Feb. 12: The FDA approved G1 Therapeutics, Inc.'s Cosela*** (trilaciclib) to decrease the incidence of chemotherapy-induced myelosuppression in adults when administered

dominate in the future as new treatments, including cancer vaccines, as well as new and expanded indications, are approved at a pace that is often difficult to keep up with. Neurology, immunology and rare diseases also have very promising" pipelines. Ultimately, says Mourad, "manufacturers, payers and other stakeholders can collaborate to further promote market access and deliver patient care, and this includes clinical program development between payers and providers, as well as innovative contracting opportunities."

For more information, contact Agarwal and Corvino through Ellen Conti at elconti@deloitte.com, Mourad through Tess Rollano at trollano@coynepr.com and Stoll through Bill Borden at wborden@kpmg.com. ✧

New FDA Specialty Approvals *(continued)*

prior to a platinum/etoposide-containing regimen or topotecan-containing regimen for extensive-stage small cell lung cancer. The agency gave the kinase inhibitor priority review and breakthrough therapy designation. The recommended dose is 240 mg/m^2 via a 30-minute intravenous infusion completed within four hours before the start of chemotherapy on each day that chemotherapy is administered. Visit https://cosela.com.

✦ ***Feb. 22: The FDA expanded the use for Agilent Technologies Inc.'s PD-L1 IHC22C3 pharmDx assay*** to identify people with NSCLC with tumor programmed death ligand-1 (PD-L1) expression of tumor proportion score ≥ 50% who may be candidates for treatment with Libtayo (see below brief). It is the only companion diagnostic the FDA has approved for this use. Visit https://bit.ly/37LbKju.

✦ ***Feb. 22: The FDA gave an additional indication to Libtayo*** for the first-line treatment of people with advanced NSCLC whose tumors have high PD-L1 expression of tumor proportion score ≥ 50%, as determined by an FDA-approved test (see above brief). Patients must have either metastatic or locally advanced tumors that are not candidates for surgical resection or definitive chemoradiation, and the tumors much not have EGFR, ALK or ROS1 aberrations. The agency gave the drug priority review for this indication. Dosing of the PD-1 inhibitor is 350 mg as a 30-minute intravenous infusion every three weeks. Visit www.libtayo.com.

✦ ***Feb. 24: The FDA expanded the approval for AbbVie Inc.'s Humira*** (adalimumab) to include the treatment of moderately to severely active ulcerative colitis in people at least 5 years old. The agency first approved the tumor necrosis factor inhibitor on Dec. 31, 2002. Dosing of the subcutaneous injectable for the newest indication is based on weight. Website GoodRx lists the price of two 40 mg/0.4 mL pens as more than $5,800. Visit www.humira.com.

✦ ***Feb. 25: The FDA gave accelerated approval to Sarepta Therapeutics, Inc.'s Amondys 45*** (casimersen) for the treatment of Duchenne muscular dystrophy (DMD) in people with a confirmed mutation amenable to exon 45 skipping. The agency gave the drug priority review, as well as fast track and orphan drug designations. Dosing for the intravenous infusion is 30 mg/kg of body weight once weekly over 35 to 60 minutes via an in-line 0.2 micron filter. The company says the drug is priced at parity with its other DMD therapies, which are around $300,000 per patient per year. Visit https://amondys45.com.

✦ ***Feb. 26: The FDA granted accelerated approval to Oncopeptides AB's Pepaxto*** (melphalan flufenamide) in combination with dexamethasone for the treatment of adults with relapsed or refractory multiple myeloma who have received at least four lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent and one CD38-directed monoclonal antibody. The company says it is the first FDA-approved anticancer peptide-drug conjugate. The recommended dose is 40 mg as a 30-minute intravenous infusion on the first day of each 28-day treatment cycle in combination with dexamethasone. Visit https://bit.ly/3q5ImuO.

✦ ***Feb. 26: The FDA approved Origin Biosciences, Inc.'s Nulibry*** (fosdenopterin) to reduce the risk of death due to molybdenum cofactor deficiency Type A. The agency gave the drug priority review, as well as breakthrough therapy, orphan drug and rare pediatric disease designations. The company also received a rare pediatric disease priority review voucher. Dosing is weight-based and varies by age. Visit www.nulibry.com.

Three CAR-Ts Are in NHL Space

continued from p. 1

Breyanzi — previously known as liso-cel, the shortened version of its non-proprietary name — joins Novartis Pharmaceuticals Corp.'s Kymriah (tisagenlecleucel), first approved in August 2017 *(RSP 9/17, p. 4)*, and Yescarta (axicabtagene ciloleucel) from Gilead Sciences Inc. unit Kite Pharma, Inc., approved in October 2017, as the three CAR-T therapies in NHL. Kymriah also is approved to treat people up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

"We never would have dreamed about five or six years ago that there would be competition in the space," said Lynn Nishida, R.Ph., chief pharmacy officer and managing partner at Trend HealthCare Partners, during a Feb. 11 webinar. But now "we have even more options using this highly complex technology."

For the Managed Care Oncology Index: Q2 2020, between June 1, 2020, and June 30, 2020, Zitter Insights polled 51 commercial payers with 129.6 million covered lives. Those with 96% of lives anticipated that they would manage Breyanzi to label. Asked how impactful its introduction into NHL would be for their management of the indication, payers with 71% of lives said it would have either no impact or minimal impact, while 28% said it would have a moderate impact.

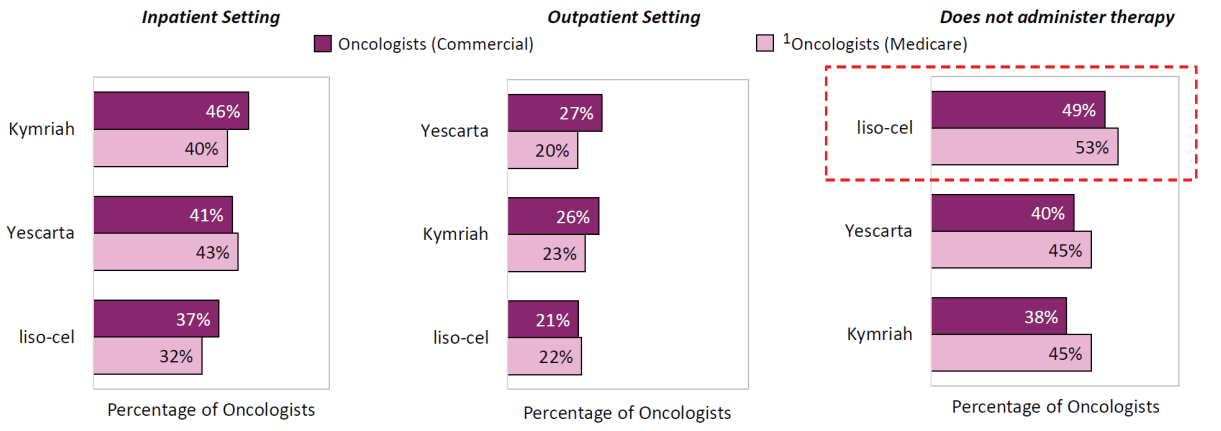
AIS Health and Zitter Insights are both MMIT companies.

Payers said that Breyanzi would need to have a 15% to 16% reduction in its wholesale acquisition cost from the WACs of the other two CAR-Ts for members to have access to the new agent. Breyanzi launched with a list price of $410,300 for the one-time treatment compared with $373,000 for Yescarta and Kymriah in NHL. The price for Kymriah in ALL is $475,000.

In response to a question about the new drug's price, Kimberly Whitefield, director of worldwide cell therapy communications at BMS, tells AIS Health that "Breyanzi is a potentially definitive treatment with a differentiated safety and efficacy profile for R/R LBCL [i.e., relapsed/refractory large B-cell lymphoma] that addresses an unmet need by offering an individualized treatment experience for patients and HCPs [i.e., health care professionals]. Breyanzi can be administered in the inpatient or outpatient setting of a certified health care facility and has demonstrated sustained response. BMS believes Breyanzi delivers significant value including medical value, patient value and overall impact to the health

Approximately one-half of oncologists are unlikely to administer liso-cel once available for their Commercial or Medicare patients

ONCOLOGISTS' ANTICIPATED SITE OF ADMINISTRATION FOR CAR-T THERAPIES ASSUMING APPROVAL OF LISO-CEL



Oncologists N = 102, [1]Oncologists n = 93
Q: "Assuming approval of lisocabtagene maraleucel (liso-cel), please indicate your likely administration of the following CAR-T therapies (Kymriah, Yescarta, and liso-cel) in the following settings for your commercial/[1]Medicare patients. Please select all that apply."

Surveys collected 6/1/2020 – 6/30/2020

SOURCE: Zitter Insights, Managed Care Oncology Index: Q2 2020.

care system. BMS prices our therapies based on the value they deliver. In setting the price for this new treatment, we considered many factors to ensure responsible pricing that strikes a balance between ensuring access for every eligible patient who may benefit and rewarding medical innovation and investment in research and development."

Will Competition Result In Price Erosion?

"All three CAR-T therapies have the same approved indication for relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy," points out Winston Wong, Pharm.D., president of W-Squared Group. "One would think that this would lead to increased competition for the lymphoma indication, leading to the potential ability for payers to negotiate net pricing. I believe the reality is that unless the managed care organization has a pathway program in place, there will be few organizations that will manage the selection of any of the CAR-T agents for the lymphoma indication. Only those organizations with a pathway program in place will truly manage the class. Since efficacy and safety appear to be similar across the three CAR-T agents, it will come down to cost. Perhaps with three CAR-Ts on the market for the same indication, one can only hope to see some price erosion."

BMS is not offering outcomes-based contracts at this time, Whitefield says, but it does offer programs and resources for patients and their caregivers, including "copay assistance for patients with commercial/private insurance, a patient assistance program for eligible patients with financial need who are uninsured or have insurance that excludes coverage for [the] CAR-T cell therapy product and assistance for eligible patients with financial need who must relocate to comply with safety monitoring requirements."

Providers May Drive CAR-T Choice

Wong tells AIS Health that "it is my expectation that the oncology practice will be the deciding party to choose a preferred CAR-T, based upon experience and cost to the practice."

Zitter Insights also polled 102 oncologists between June 1, 2020, and June 30, 2020. Approximately half said they did not anticipate administering Breyanzi, slightly more than those with the same response for Yescarta and Kymriah (see chart, p. 10). Of oncologists administering the CAR-Ts, more expected to do so in an inpatient setting as opposed to an outpatient one. One of the reasons for hesitancy over outpatient infusion is the products' side effect profile. The labels for all three therapies contain black-box warnings for neurologic toxicities and cytokine release syndrome (CRS), a potentially fatal reaction that is treated with Actemra (tocilizumab) from Roche Group member Genentech USA, Inc.

Asked how payers can distinguish among the CAR-Ts, Wong responds that "most payers will have medical policies in place that will state that the medication is to be used for its approved label. Due to the complexity of the CAR-T administration, as well as administration in a certified facility, payers will be most likely aware of the utilization of any of the CAR-T agents, but this will mainly be from a contracting standpoint as opposed to the promotion of a preferred product."

BMS says it can turn around a dose of the product within 24 days. That's slightly more than the other two CAR-Ts, which may be a "disadvantage" for Breyanzi, said Nishida during the webinar: Kymriah takes 22 days, and Yescarta takes 17 days. Clinical trials showed a complete remission rate of 54% for people treated with Breyanzi, "which is on par" with Yescarta, she said, and Kymriah for the same indication has a 64% remission rate. All three therapies require that patients are monitored closely for a period of time after infusion, with the requirement that patients remain near the treatment facility for a period of time.

BMS Is Providing Wearable Technology

For the first week following infusion with Breyanzi, patients will be monitored daily, which may be done in person or remotely, and then must stay "within proximity" of the health care facility for at least four weeks after infusion, says Whitefield. BMS is providing Cell Therapy 360, "a digital service platform that optimizes access to relevant resources which are designed to support patients and caregivers through the Bristol Myers Squibb CAR-T cell therapy journey, from enrollment through the initial post-infusion monitoring period. The platform includes outpatient monitoring support. BMS will also offer patients disposable wearable technology during the initial post-infusion monitoring period, which will help them track their temperature in real-time through a smartphone."

Asked how BMS will conduct long-term patient monitoring, Whitefield says that both long- and short-term care "will vary by patient.… Supportive care or treatment may be required to manage CRS, neurologic events or other potential adverse events following treatment with Breyanzi. As part of the 15-year follow-up registry study, patients who receive Breyanzi will require long-term monitoring in order to characterize the long-term safety profile of Breyanzi in the

post-marketing setting. In addition, lifelong monitoring should be conducted to identify potential secondary malignancies."

Payer preparation for these treatments cannot come too quickly, with FDA decisions on more CAR-Ts expected soon. Nishida pointed out that a decision on BMS's multiple myeloma therapy idecabtagene vicleucel could come by the end of this month. Another multiple myeloma treatment, Johnson & Johnson's citacabtagene autoleucel, has a decision expected in the second half of this year.

"Regardless of the high price, it just really spells out how payers need to be prepared to address these high-cost products for the rare few who have little options left, but they could potentially benefit from these products," said Nishida.

For more information on the Zitter data, contact Jill Brown Kettler at jbrown@aishealth.com. Contact Nishida at Lynn.Nishida@TrendHCP.com, Whitefield at Kimberly.Whitefield@bms.com and Wong at w2sqgroup@gmail.com. ✧

News Briefs

✦ ***AstraZeneca said Feb. 22 that it would voluntarily withdraw the Imfinzi (durvalumab) indication in the U.S. for previously treated adults with locally advanced or metastatic urothelial carcinoma*** who have disease progression during or following platinum-containing chemotherapy or who have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy. The FDA gave the indication accelerated approval on May 1, 2017 *(RSP 5/17, p. 10)*. A confirmatory trial did not meet post-marketing requirements. View the statement at https://bit.ly/3kF92RO.

✦ ***Merck & Co., Inc. said March 1 that it was voluntarily withdrawing the U.S. indication for Keytruda (pembrolizumab) for the treatment of patients with metastatic small cell lung cancer*** with disease progression on or after platinum-based chemotherapy and at least one other line of therapy. The FDA gave the drug accelerated approval on June 18, 2019, for the indication *(RSP 7/19, p. 8)*. The company was required to conduct a post-marketing study to establish superiority of the drug as determined by overall survival. The confirmatory Phase III trial had two primary endpoints; the drug met the progression-free survival endpoint but did not reach statistical significance for the overall survival endpoint. The move comes just a few months after Bristol Myers Squibb said on Dec. 29, 2020, that it was withdrawing the exact same indication for Opdivo (nivolumab) following accelerated approval on Aug. 17, 2018 *(RSP 1/21, p. 12)*. View Merck's statement at https://bit.ly/2NKEe6t.

✦ ***AlohaCare entered into a three-year pharmacy benefits management deal with IngenioRx*** that starts July 1. IngenioRx, which Anthem, Inc. launched in October 2017, will provide services for the community-led Medicaid and dual eligible Medicare insurer's members in QUEST Integration, a Medicaid managed care program. Contact Anthem's Lori McLaughlin at lori.mclaughlin2@anthem.com.

✦ ***PBM Navitus Health Solutions' wholly owned specialty pharmacy, Lumicera Health Services, purchased specialty pharmacy CareMetx Health*** from hub services company CareMetx. Navitus, whose specialty pharmacies are located in Madison, Wis., and Phoenix, says the new company, which is located in Gaithersburg, Md., will allow it to better serve patients in the eastern U.S.…In other Navitus news, the company strategically invested in medication guidance company WithMe Health, Inc. WithMe offers a personalized approach that leverages data-driven member information with a pharmacist-led medication guidance team. Navitus is owned by SSM Health and Costco Wholesale Corp. Contact Navitus at Navitus@AllisonPR.com.

✦ ***The Health System Owned Specialty Pharmacy Alliance's (HOSP) board of directors maintained that "we need industry-wide benchmarks*** to both demonstrate our success and measure our performance to further improve patient outcomes" in a recent open letter to the integrated specialty pharmacy industry. HOSP formed last year to advocate for integrated specialty pharmacies *(RSP 11/20, p. 6)*. The letter also called for the industry to support patient choice and open access, as well as prioritize health equity. Read the letter at https://bit.ly/304N29J.