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Navigating Provider Challenges to Growth of The CAR T-Cell Therapy Space

INTRODUCTION

Chimeric antigen receptor (CAR) T-cell therapy represents a major advancement in personalized cancer treatment. An intersection of immuno-oncology and gene therapy, a patient's own T-cells are genetically engineered to express a synthetic receptor that binds a tumor antigen. CAR T-cells are then expanded for clinical use and infused back into the patient's body to attack and destroy chemotherapy-resistant cancer. In 2017, the first two CAR T-cell therapies were approved in the US—Kymriah (tisagenlecleucel), from Novartis, for the treatment of pediatric and young adult patients with B-cell precursor acute lymphoblastic leukemia (ALL) and Yescarta (axicabtagene ciloleucel), from Gilead / Kite Pharma, for the treatment of adult patients with relapsed or refractory large B-cell lymphoma. The launches were hailed as transformational; the first successful examples of synthetic biology and personalized cellular cancer therapy to become commercially available. Yet today, no more than 100 hospitals in the US have been certified to provide CAR T-cell therapy, while far fewer have actually administered the therapy to a patient. Herein we explore the challenges that have limited the growth of facilities offering CAR T-cell therapies, focusing on federal, state and commercial payer as well as intra-institutional considerations that have limited adoption and growth.

FEDERAL CONSIDERATIONS

CMS Reimbursement for Inpatient Treatment is a Negative Sum Game for Hospitals - In early August, the Centers for Medicare & Medicaid Services (CMS) released a National Coverage Determination (NCD) for FDA-approved Chimeric Antigen Receptor T-cell (CAR T-cell) Therapy, impacting both reimbursement of and coverage for CAR T-cell therapies. Medicare will cover CAR T-cell therapies when they are provided in healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies (REMS) for FDA-approved indications (according to the FDA-approved label). In addition, Medicare will cover FDA-approved CAR T-cell therapies for off-label uses that are recommended by CMS-approved compendia. The NCD continues coverage for routine costs in clinical trials that use CAR T-cell therapy as an investigational agent that meet the requirements listed in NCD 310.1. CMS refrained from creating a new DRG for CAR T-cell therapies at launch, but rather within the final Inpatient Prospective Payment System (IPPS) rule, published on August 2, 2019, CMS followed the more usual process of creating an add-on payment (NTAP) to account for the cost of the therapeutic, coupled with a DRG

(016-autologous bone marrow transplant) that roughly matches the likely effort involved with the procedure. In doing so, they cited a need for more data to justify a new MS-DRG. Under its final FY 2020 rule on payment, CMS included revisions to the calculation methodology for new technology add-on payments (NTAP), including a higher NTAP overall. Under previous regulations, Medicare made add-on payments equal to the lesser of either 50% of the costs of the new medical service or technology, or 50% of the amount by which the costs exceed the standard DRG payment. The FY 2020 rule increases the NTAP amount to either 65% of the costs of the new medical service or technology or 65% of the amount by which the costs exceed the standard DRG payment. While the revisions to NTAP calculations was certainly better than before, the 15% increase is unlikely to come anywhere close to covering the price of certain high-cost therapies, including CAR T-cell therapy. Indeed, the add-on payments (NTAP) for CAR T-cell therapies, from 50% to 65%, translates to a mere $186,500 (Yescarta) to $242,450 (Kymriah). However, this does not include hospitalization and other costs. Given patient management (which can go as high as, and sometimes beyond, $0.5 million), the reimbursement gap remains unsustainable to institutions and a huge impediment to patient access. Indeed, it has been calculated that hospitals can lose upwards of $100,000 per patient when they provide CAR T-cell therapy to a Medicare beneficiary on an inpatient basis.

CMS Reimbursement for Outpatient Care, While in Itself Net Positive, Expose Hospitals to Risk - In contrast to inpatient care, CMS reimburses hospital outpatient care roughly the wholesale acquisition cost (WAC) plus 6%. That amounts to $395,380 to those who administer Yescarta on an outpatient basis and $500,839 for outpatient treatment with Kymriah. Out-of-pocket expenses for Medicare patients are capped at around $1,340 plus their Part B deductible ($185 for 2019) if it hasn't been met. Although reimbursements for patients who receive CAR T-cell therapy and do not require inpatient monitoring for toxicities allow the hospital to profitably treat some patients and bank that revenue to subsidize patients who require post-infusion inpatient care, the strategy can be risky for the patient and provider alike. If medical treatment is initiated in an outpatient setting and the patient needs inpatient care within 72 hours, all payments prior to that 72-hour window become part of the inpatient stay. However, current CAR T-cell therapies have been associated with unique adverse events (AEs), including cytokine release syndrome (CRS) and neurologic events (also known as CAR T-cell–related encephalopathy syndrome (CRES) or, immune effector cell–associated neurotoxicity syndrome (ICANS) that can lead to extended inpatient care. A published review of costs found that adult patients who receive CAR T-cell therapy have a median hospital stay of 15 days, at a median cost of more than $85,000. For patients under the age of 25, the median hospital stay is 19 days, with a median total cost of more than $242,000. Given the potential cost savings if hospitalization can be reduced or avoided altogether, reduction of AEs is emerging as a crucial economic differentiator in the value story of numerous CAR T-cell therapies in development

Value-based Reimbursement has Made Slow and Uncertain Progress in the US - Value-based reimbursement models that include bundled payments, pay-for-performance, shared savings and other features, can significantly complicate the order-to-cash process. Novartis initially offered outcomes-based pricing for Kymriah (only for the treatment of B-Cell Acute Lymphoblastic Leukemia) — an agreement that tied the therapy's clinical success to its payment. Notably, this arrangement did not include the hospital expenses associated with the therapy. The payment deal was suspended in July of 2018 after it drew internal Health and Human Services scrutiny and became the target of congressional investigations.

STATE CONSIDERATIONS

Certificate of Need Restrictions Have Been Attempted in Michigan to Limit Hospitals From Offering CAR T-Cell Therapy - On Sept. 19, the state Certificate-of-Need (CON) Commission unanimously approved a regulation that would require hospitals to go through a third-party accreditation processes before being able to offer CAR T-cell therapies. This was subsequently struck down by the Michigan Legislature on October 30. Even after obtaining that additional accreditation, hospitals would have needed to come back to the CON commission for another approval—a process that effectively means only large, wealthy, hospital-based cancer centers will be able to offer the treatments. Though the specific applications of CON laws differ from state to state, their stated purpose is to prevent overinvestment and keep hospitals from having to charge higher prices to make up for unnecessary outlays of capital costs. Michigan is one of 35 states that have CON laws, which are intended to decrease duplication and promote health care consolidation. Although most CON law disputes involve the construction or expansion of physical facilities, they also apply to new treatments and services provided by clinics and hospitals.

Medicaid Coverage is Variably Restrictive Across States – Not all Medicaid programs cover CAR T-cell therapy, with finite resources, leading to variably restrictive policies that vary from state to state. Our review of online state Medicaid agency websites reveal just 15 states with an accessible Kymriah policy (AZ, CA, CT, FL, IA, KS, MN, MO, MT, NY, OK, RI, UT, VT, WV), of which, with the exception of IA, MN, UT,VT (11 states) provide an accessible Yescarta policy. Kymriah and Yescarta are predominantly managed by prior authorization with the exception of Minnesota and Utah[1] which maintain quantity limits and Missouri which has instituted a step edit.

COMMERCIAL PAYER CONSIDERATIONS

The Uncertainties of CAR T-cell Therapy Inherently Favor Larger Institutions in Commercial Reimbursement – As CAR T-cell therapy has remained relatively rare, hospitals have been brokering one-off arrangements with private insurers. While coverage refusal is rare, the challenges of predicting patient adverse event reactions to CAR T-cell therapy and consequent care, based on limited patient experience, have left hospitals challenged to estimate the final cost of treatment and calculate the break-even of reimbursement. A lengthy, resource intensive and uncertain process that may stretch settlement by months, these risks inherently favor larger institutions with a greater ability to spread risk and resources by volume of CAR T-therapy patients and other treatment modalities. Volume additionally favors larger institutions, as once a hospital has navigated reimbursement with a payer, consequent arrangements have been found less burdensome to execute. A doubled-edged sword, larger institutions are nonetheless concerned over their reimbursement exposure to CAR T-cell therapies, particularly given a combination of potential patient access and CAR T-cell indication growth, despite break-even challenges among the current indications.

[1] Quantity limits in Utah refer only to Kymriah, as a policy for Yescarta was not found

INTRA-INSTITUTIONAL CONSIDERATIONS

Accountability During "Vein to Vein Time" Lacks Clarity - Site-of-care administrators lack immediate clarity as to the cost liability to the institution and payer if the patient expires before the medication can be administered. A period known as "vein to vein" time occurring in the window where blood is drawn, transported, processed and subsequently returned to the hospital for reinfusion.

Cash Flow Cycles Remain Long - The reimbursement cycle is longer as providers are being asked to follow multiple, complex order-to-cash processes; while taking on significant risk for floating the costs of high cost medications as they await reimbursement. Many hospitals do not have the ability to fully absorb the cash flow burden of these medications for a long period of time. This is exacerbated by the high therapy cost and complicated payer policies that divert limited administrative resources.

Burden of Accreditation and Training Limits Potential Facilities to the Largest Academic Centers – The national coverage determination mandates CAR T-cell therapies be available only through a restricted and regulated program, in certified centers and administered by trained healthcare providers. In addition, the healthcare facility must be enrolled in the FDA Risk Evaluation and Mitigation Strategies (REMS) program for FDA-approved indications. Training of HCPs is a mandatory step toward getting a center certified as a CAR T-cell specialist center. The long training process and the increasing demand for CAR T-cell therapies, however, are increasing patient waiting lists as new centers await certification. To this end, the process of developing a sustainability plan as well as training physicians and nurses can be lengthy and resource intensive as staff from across the facility must be trained.

Patient Pool can be Limited by Indication and Referral System - Indications for CAR T-cells are limited to heavily pre-treated patients. Patients must have progressed on at least two lines of systemic therapies to be eligible for Kymriah or Yescarta treatment. Consequently, the eligible patient pool is further limited to heavily pretreated patients with good performance status. Notably, in its national coverage determination, Medicare will cover FDA-approved CAR T-cell therapies for off-label uses that are recommended by CMS-approved compendia. Yet, there is inherent complexity in the patient referral pathway that limits a hospital's eligible patient pool. Primary care oncologists must refer eligible patients to CAR T-cell therapy specialists, a process that hinders the widespread adoption of CAR T-cell therapy. Contributing to this headwind, there is lack of clarity in the placement of CAR T-cell therapy in oncology treatment practices.

CLOSING REMARKS

Tempered by these challenges, the US CAR T-cell therapy market is nevertheless estimated to approach $3 billion by 2026, driven both by indication expansion of existing therapies and a rapidly evolving landscape of new CAR T-cell therapies targeting antigens in both liquid and solid tumors. For context, global estimates of emerging CAR T-cell therapies alone indicate 250+ preclinical and ~300 clinical stage agents in development, a ~40% increase from the year before. The larger cell therapy space is estimated at 500+ preclinical and just under 500 clinical stage agents. As a leading healthcare-focused advisory firm, Marwood advises a variety of biopharma, diagnostic and device companies as well as healthcare investors in conducting market diligence, strategizing market access and managing product life cycles leveraging direct insight into federal and state policy as well as intra-institutional dynamics.

About the Author

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