

# Unravelling the CAR T-cell therapy reimbursement riddle

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Physicians may finally have some clarity on payment for inpatient administration of 2 chimeric antigen receptor (CAR) T-cell therapies if a proposed rule from the Centers of Medicare & Medicaid Services becomes final.

The agency is seeking to assign ICD-10-PCS codes XW033C3 and XW043C3 to the use of axicabtagene ciloleucel (Yescarta; Kite Pharma, acquired by Gilead in October 2017) and tisagenlecleucel (Kymriah; Novartis) in the inpatient setting for fiscal year 2019. It is also considering the creation of a new Medicare Severity-Diagnosis Related Group (MS-DRG) code for procedures involving the use of CAR T-cell therapy drugs.

Stephanie Farnia, director of health policy and strategic relations for the American Society for Blood and Marrow Transplantation, said the proposal demonstrates that CMS is listening to physicians' concerns about CAR T payments and working to provide a more reasonable framework. "The primary point of significance is that CAR-T care episodes should be assigned to a specific MS-DRG in FY2019, which will give physicians a clearer sense of inpatient reimbursement in advance," she said in an interview.

Uncertainty about inpatient payment for administration of the 2 approved CAR T therapies (see p. e126) have been a lingering concern of specialists who use, or are interested in using, the therapies. In April 2018, CMS announced payment rates for outpatient administration of the 2 drugs, settling on \$395,380 for axicabtagene ciloleucel and \$500,839 for tisagenlecleucel. The two medications have list prices of \$373,000 and \$475,000, respectively.

However, physicians noted at the time that even if the drugs were first administered in the outpatient setting, inpatient care is likely to occur with CAR T-cell therapies because some patients will need to

be admitted for monitoring for serious side effects. In such cases, all payments would then become part of the inpatient stay as per CMS's 3-day payment window rule.

In the most recent payment proposal, CMS stated that its clinical advisers believe that patients receiving treatment with CAR T-cell therapy would have similar clinical characteristics and comorbidities as

patients treated with autologous bone marrow transplant therapy, who are currently assigned to MS-DRG 016 *Autologous Bone Marrow Transplant with CC/MCC*. Therefore, CMS officials said they would suggest ICD-10-PCS procedure codes XW033C3 and XW043C3 to pre-MDC MS-DRG 016. In addition, the agency is proposing to revise the title of MS-DRG 016 to *Autologous Bone Marrow Transplant with CC/MCC or T-cell Immunotherapy*.

The agency emphasized that it invites public comment on alternative payment approaches for CAR T-cell therapies in the context of the

pending, new technology add-on payment applications by the CAR-T drugmakers Novartis and Kite Pharma/Gilead. If approved, the technology add-on payments would provide an additional and separate payment equivalent to up to 50% of the product cost plus the MS-DRG payment received for the episode of care.

## Shifts and realignments in the face of new developments

The CMS announcement is the latest development in the rapidly growing landscape of CART-cell therapies. In 2017, the Food and Drug Administration approved tisagenlecleucel for pediatric acute lymphoblastic leukemia and axicabtagene ciloleucel for relapsed/refractory large B-cell lymphoma in adults, and in May 2018, the agency expanded the indication for tisagenlecleucel to include adults with



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relapsed/refractory large B-cell lymphoma.

Further advancements are expected for CAR T-cell therapies in 2018, said Cai Xuan, PhD, senior analyst in oncology and hematology for GlobalData, a data analytics and commercial intelligence firm.

For starters, pharmaceutical companies are now working toward next-generation CAR T-cell therapies that can be mass produced, Dr Xuan noted. At a recent American Association for Cancer Research meeting, for example, the biopharmaceutical company Collectis presented early clinical data in pediatric B-cell acute lymphoblastic leukemia for its off-the-shelf CAR T-cell candidate UCART19. In addition, CRISPR Therapeutics presented preclinical data for one of its off-the-shelf CAR T-cell candidates for multiple myeloma, and the company announced it would apply for approval to start human trials by the end of 2018.

“The trend for 2018 is focused on how to eliminate some of the profitability issues with first-generation CAR Ts because companies realize that manufacturing individualized treatments for each patient is not an ideal business model,” Dr Xuan said in an interview.

More market competition is also in the forecast, particularly from smaller companies, Dr Xuan said. “We are likely to see larger companies acquiring smaller ones once their CAR T technology has matured to a certain point. We have seen it with the Gilead-Kite acquisition and Celgene’s acquisition of Juno Therapeutics. This trend will continue as long as smaller companies are able to develop proprietary next-generation CAR T technologies.”

#### **Cost, accessibility, and real-world side effects**

The key concerns about the therapies are cost and accessibility, especially for the Medicare population. Cost estimates have put the cost of CAR T-cell therapies as high as \$1.5 million per patient and that could make them inaccessible for many.

“There remain unanswered questions about value and cost in older adults,” said Walid F Gellad, MD, codirector for the Center for Pharmaceutical Policy and Prescribing at the University of Pittsburgh. “There are many life-saving

treatments in the medical system that cost much less than this therapy. Presumably, its cost will go down as the indications expand and the experience with creating the CAR T cells improves. At least, one would hope.”

The creation of off-the-shelf, third-party products would help improve accessibility for CAR T-cell therapies and lower cost, said Helen Heslop, MD, director of the Center for Cell and Gene Therapy at Baylor College of Medicine, Houston. “In the longer term, there’re obviously a lot of people looking at how [the treatments] can be made more accessible. These are the first-generation CAR T [products], and I think there’ll be lots of refinements both to make them more effective and safer and also to use a third-party product to bring the cost of goods down.”

Other lingering unknowns about CAR T-cell therapies include how many patients in real-world clinical practice will have serious side effects, compared with those in trials, and the long-term recurrence rates after therapy use, Dr Gellad noted. He recently proposed in an article that government payers reimburse only the cost of manufacturing and some predetermined mark-up for such therapies until confirmatory trials demonstrate clinical benefit (*N Engl J Med.* 2017;376[21]:2001-4).

The current CAR T-cell therapies are only the beginning, said Dr Richard T Maziarz, MD, a bone marrow transplantation and blood cancer specialist at the Oregon Health and Science University Knight Cancer Institute in Portland. “Genetically engineered cell products are going to explode over the course of the next decade. This is not the end of the line, this is the starting point.”

#### **Disclosures**

Dr Maziarz has received consulting fees from Novartis, Juno Therapeutics, and Kite Pharma. Dr Heslop has received consulting fees from Novartis, has conducted research for Cell Medica and holds intellectual property rights/patents from Cell Medica, and has ownership interest in ViraCyte and Marker Therapeutics. Dr Gellad reports grants from Express Scripts.