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November 1, 2017

Ms. Amy Bassano and Ms. Arrah Tabe-Bedward
Center for Medicare & Medicaid Innovation
Centers for Medicare & Medicaid Services
Department of Health and Human Services,
Mail Stop C4-26-05,
7500 Security Boulevard,
Baltimore, MD 21244-1850.

CC: Chris Ritter, Mary Kapp, Ellen Lukens, Will Robinson, Ron Kline

RE: Request for CMS to Invoke CMMI Authority for CAR-T Drug Reimbursement for Medicare and Medicaid Patients

Ms. Bassano and Ms. Tabe-Bedward:

The American Society for Blood and Marrow Transplantation (ASBMT) is an international professional membership association of more than 2,200 physicians, scientists and other healthcare professionals promoting blood and marrow transplantation and cellular therapy through research, education, scholarly publication and clinical standards. ASBMT is dedicated to improving the application and success of hematopoietic cell transplants and/or other cellular therapies, such as CAR-T.

Hematopoietic cell transplantation (HCT) is a medical sub-specialty comprised of physicians with Board Certifications in Internal Medicine, Medical Oncology, Pediatrics, Hematology and/or Immunology. CMS recognized the unique role and qualifications of HCT physicians by designating a unique code for Hematopoietic Cell Transplant and Cell Therapy (HCTCT) physicians in November 2016.[1] Due to their unique clinical expertise and training, ASBMT member clinicians and cellular therapy programs will be the primary individuals and teams initially providing Chimeric Antigen Receptor T Cell Therapy (CAR-T) to patients in need of treatment. We anticipate that CAR-T is the first of many engineered cellular therapies to be approved in the coming decade.

[1] CMS MLN Matters MM957

This class of therapies will require unique reimbursement considerations given their newness relative to the long-standing Medicare reimbursement systems and their anticipated costs to providers as part of providing quality care. We concur with the expert commentary labeling cellular therapies as the key breakthrough therapy of the 21st Century, as discussed at the July 13, 2017 FDA Oncology Drugs Advisory Committee.[2] Due to the involvement of our membership and the coming wave of innovation that these cellular therapies represent, the ASBMT is keenly interested in how to improve Medicare's long-standing reimbursement models so they can be applied fairly and adequately to these technologies on behalf of our members.

Summary of Request

ASBMT requests that CMS utilize its CMMI authority to immediately establish separate payment for the drug/biological expense of the CAR-T product, in addition to the usual payment made to providers for their inpatient hospital services.

Background Information

Chimeric Antigen Receptor T Cell Therapy (CAR-T) is a new category of cell-based gene therapies utilizing a patient's own immune system to treat certain hematologic malignancies. A patient's cells are collected, genetically modified to attack cancer cells and then are infused back into the patient. The Food and Drug Administration (FDA) approved the first of these genetically modified cell therapy products on August 30th; Novartis's Kymriah is aimed at treating patients (up to age 25) with relapsed or refractory pediatric acute lymphoblastic leukemia (P-ALL). A second product, Yescarta, from Kite-Gilead, received FDA approval on October 18, 2017, for treating three lymphoma subtypes, including the treatment of Diffuse Large B Cell Lymphoma, Primary Mediastinal B Cell Lymphoma and Transformed Follicular Lymphoma. The subtypes are most frequently diagnosed in those over the age of 60.

We were pleased to see Administrator Verma describe the first CAR-T product as an "*[i]nnovation[] . . . [that] reinforce[s] our belief that current healthcare payment systems need to be modernized in order to ensure access to new high-cost therapies, including therapies that have the potential to cure the sickest patients.*"

Administrator Verma has also stated that "*[t]hrough the authority provided to the Center for Medicare and Medicaid Innovation (CMMI), CMS will aim to identify and alleviate regulatory barriers in Medicare and Medicaid as may be necessary to test payment and service delivery models that involve value-based payment arrangements.*"

Predominantly Inpatient Setting

Novartis and Kite/Gilead both indicate in their product literature that CAR-T is safe to be administered in either the outpatient and inpatient setting. However, due to the extensive system of facility and provider capabilities that must be immediately available to a patient during and after the infusion of the therapy, and as the therapy is being provided to patients who are critically ill and have received multiple other prior therapies, administration of CAR-T is

[2] FDA ODAC Meeting, July 13, 2017

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expected to be provided predominantly in the inpatient setting for the immediate post-approval timeframe. Some hospitals may be able to migrate it to the outpatient setting depending upon their organizational structure once more experience is gained with this powerful new therapy.

The cost of acquiring the personalized CAR-T product is very high and is additive to the cost of the hospital services required to administer the therapy. The likely MS-DRG payments that would be assigned through the regular claims submission and reimbursement processes today would leave hospitals facing vast financial losses for direct expenses, even after factoring in outlier payments, which could ultimately impact access to care for patients.

Opportunity to Create Reimbursement Structures to Support Provider Use of CAR-T
Given the Agency's interest and support of CAR-T therapy, we believe CMS should recognize and remedy the extraordinary financial shortfall the provision of this product will cause to providers when they administer it in the inpatient setting. CMS has an existing reimbursement methodology for physician-administered drugs and biologicals in the Outpatient Prospective Payment System (OPPS) which could be invoked and used for the inpatient use of CAR-T.

We understand CMS has agreed to conduct some form of a CMMI value-based payment model for at least one of the new CAR-T products. ***We believe that either as a part of this value-based payment model, or as a unique and related payment model, separate payment for the drug/biological expense of the CAR-T product should be made by CMS utilizing its §1115A authority (1115 authority for Medicaid). Specifically, CMMI would allow separate drug/biological inpatient ASP-based payment for the CAR-T product, in addition to the usual inpatient hospital service payment whether that occurs under the standard MS-DRG IPPS payment methodology or under the TEFRA methodology for the PPS-exempt centers.***

This structure would create payment parity across care settings and sites for the highest individual cost portion within the care episode – and that which providers have no ability to impact – the cost of the CAR-T drug itself. We ask that CMS apply its CMMI authority to both Medicare and Medicaid, as many of the impacted patients, pediatric or adult, will be participants in state Medicaid programs that would benefit from CMS' direction and guidance on the implementation of timely and appropriate reimbursement strategies for new technologies.

We believe this change in process is critical to facilitating access to this therapy across all populations that would derive clinical benefits. Allowing both PPS and PPS-exempt hospitals to access this methodology modification will allow all patient populations to access care in the setting deemed most clinically appropriate for the patient by the provider.

Throughout the remainder of this letter, we outline a rationale for why we believe CMS should make these adjustments immediately and offer our suggestions as to some of the specific mechanisms that could be utilized.

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Inadequacy of MS-DRG Payment

We believe the most likely medical MS-DRG assignments for CAR-T cases (i.e. subtypes of non-Hodgkin lymphoma with no accompanying surgical procedure) are those listed below.

Table 1: Potential MS-DRG for CAR-T Inpatient Stays Based on Current Grouper Logic

MS-DRG	MDC	Type	Title	Weights	Approximate Base Reimbursement	Geo Mean LOS
840	17	MED	LYMPHOMA & NON-ACUTE LEUKEMIA W MCC	3.0786	$16,736	7
841	17	MED	LYMPHOMA & NON-ACUTE LEUKEMIA W CC	1.6201	$8,807	4.3
842	17	MED	LYMPHOMA & NON-ACUTE LEUKEMIA W/O CC/MCC	1.1241	$6,110	2.9

MS-DRG 840 has the highest relative weight - 3.6284 - and a base reimbursement of approximately $16,736. Separate from the cost of the product, the average length of stay for Medicare beneficiaries receiving Yescarta will likely deviate substantially from the range of ALOS numbers associated with these MS-DRGs. As CMS notes in the Agency's NTAP comments in the IPPS FY18 Proposed Rule, Kite Pharma's application supplied information that indicated a median stay of 15 days.

A subset of patients that develop one of known potential post-infusion complications, including cytokine release syndrome (CRS) and/or treatment-associated neurotoxicity, will likely require hospitalization until symptoms fully resolve – potentially for up to 2-3 additional weeks. Hospital acquisition costs of Tocilizumab, used to treat CRS, were reported by member pharmacists to be $5,000-10,000 per therapeutic dose, depending on the patient, and doses may be administered several times. Assignment to one of the three identified likely MS-DRGs would be clinically inappropriate and financially devastating to providers to treat even the most routine, 'uncomplicated' CAR-T patients, not to mention those that have complications as the relative weights of these existing MS-DRGs are woefully inadequate.

Complicating this problem of inadequate inpatient reimbursement for patient care costs in FY2018 and potentially beyond, is the product cost itself. We believe CMS understands and agrees that CAR-T is a new type of biologic that is unique due its efficacy in a previously untreatable condition, as well a very high price point that cannot be decreased by provider decision-making or negotiation. Currently, there are no MS-DRGs that include reimbursement for a single drug or biologic product this expensive, and the only opportunity for hospitals to cover even part of their expense for the product, much less other patient care costs in FY2018, is through the inpatient prospective payment system (IPPS) cost outlier payment methodology. There is no new technology add-on payment available for FY2018 for either of the FDA approved CAR-T products and it remains to be seen whether a CAR-T product will achieve approval as a new technology for IPPS add-on payment for FY2019.

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Of crucial importance to note is that even with an NTAP, providers are still projected to sustain large losses if these encounters group to the expected MS-DRGs, due primarily to the expected costs of post-administration care and treatment of complications. Finally, the PPS-Exempt Centers will also be providing CAR-T to Medicare beneficiaries. Since these exempt centers are not eligible for either the NTAP or outlier payments, they too will see huge losses on the use of this breakthrough therapy with their current payment mechanism and will also need an immediate solution.

Due to the reimbursement issues that will be associated with patient care costs beyond the product acquisition costs, and that will remain even with NTAP or other product payment, ASBMT has submitted a separate formal request (see separate letter attached) to CMS for new MS-DRGs for CAR-T, with the request that these become active in FY2019.

Inadequacy of Outlier Payments

For hospitals paid under the IPPS, the cost outlier formula will be the only method available to obtain payment to cover a portion of actual case cost for FY2018. Therefore, it is important to understand the projected impact of the outlier calculation with a high cost drug. As the Yescarta drug is most applicable to the Medicare population, the remainder of our letter and the examples that follow use Kite/Gilead's published price of $373,000.

The hospital will pay the manufacturer $373,000 for the product and will then need to represent this direct cost to CMS on its inpatient claim in the form of a dollar charge. Due to the extremely high cost, hospitals will be very reluctant to mark-up the CAR-T product in the same way it does for other drugs. As CMS is aware, providers vary in their mark-up practices for drugs, devices, supplies, and all other services and this fundamentally impacts Medicare's "view or estimation" of provider cost, as well as a provider's ability to avail itself of an outlier payment. Below we provide a simple illustration of how two different hospitals could report their billed charge to CMS and what CMS would calculate as an estimated cost of Yescarta.

Example 1: Hospital A submits a billed charge of $410,300 which reflects a 10% mark-up above the publicly stated price of $373,000. Hospital B submits a significantly higher billed charge of $1,492,000, which represents a 400% mark-up and reflects its overall cost-to-charge ratio of 0.25, developed from an understanding of CMS' rate-setting and outlier payment methodologies.

Example Hospital Mark-Ups and CMS' Calculated Cost					
Example Hospital	Billed Charge	Hospital's CCR	CMS' Calculated	Actual Invoice Cost	Shortfall
Hospital A	$410,300	0.25	$ 102,575	$373,000	$ (270,425)
Hospital B	$1,492,000	0.25	$ 373,000	$373,000	$ -

As this example illustrates, if a hospital does not use its overall CCR to mark-up the invoice cost (i.e., like Hospital A), CMS will not estimate the drug cost anywhere near the actual invoice cost.

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This creates two substantial issues for both the providers and CMS. First, the hospital will be face significant losses on the drug itself. Second, if CMS uses this claim in future rate-setting, it would severely underestimate the actual cost of Yescarta, resulting in setting inappropriately low future payment rates that would impact all providers of this type of therapy. The table below shows how the IPPS cost outlier formula would work for Hospital A, using the 10% mark-up. It is important to remember that the calculation is not based on individual drugs and/or line items, but is a summation of the total charges for a category of care during the stay. Yescarta's costs with the minimal mark-up are shown in the amount reported on the Revenue Code 0250 line and, on a real claim, this would be summed together with other drugs utilized during the patient stay.

Hospital A Example CAR T Inpatient Hospital Claim			
			FL04 = 0111
FL12 = Admit Date 10-1-17		FL17 = Discharge Date 10-15-17	
FL 42 Revenue Code	FL 43 Description	FL 46 Units	FL 47 Total Charges
0121	Room & Board	14	$ 49,000.00
0250	**Pharmacy***	**101**	**$ 420,300.00**
0270	Supplies	20	$ 1,500.00
0300	Laboratory	520	$ 50,000.00
0940	Other Tx Services	1	$ 3,500.00
0001	Total Charges		$ 524,300.00
*The CAR T charge of $410,300 based on a 10% mark-up is included with other drug charges billed under revenue code 0250.			

For this inpatient hospital claim example, the total billed charges are $524,300. This amount is what is used to determine the IPPS outlier payment amount as illustrated below:

Hospital A Example CAR T Inpatient Operating Outlier Calculation	
Example MS-DRG 840 Base Payment	$ 16,736.00
FY2018 Outlier Threshold	$ 26,713.00
Example Hospital Operating CCR	0.2500
Total Charges from Inpatient Claim	$ 524,300.00
Calculated Hospital Cost (Charges * CCR)	$ 131,075.00
Outlier Threshold (MS-DRG Pmt + Threshold)	$ 43,449.00
Outlier Payment (Cost minus threshold *80%)	$ 70,100.80
Total case payment (MS-DRG Payment Plus Outlier)	$ 86,836.80

In this outlier calculation example, we have Hospital A's Yescarta CAR-T case grouping to MS-DRG 0840, which has a national unadjusted base payment of $16,736. As a result of the outlier calculation, the total case payment does increase to $86,836.80. However, this remains woefully

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inadequate to cover both the invoice cost of the CAR-T drug along with the entire inpatient admission. The inpatient admission could be anywhere from a week to a month, if CRS or other complications occur.

As the calculation above shows, Hospital A cannot receive an appropriate outlier payment if utilizing a marginal mark-up for the CAR-T product. Providers have expressed a strong concern with the idea of using significant mark-up for drugs that are this expensive, as they believe marking up drugs beyond a nominal level would be inappropriate and can create controversy among patients, payers, and the media.

Even for Hospital B, who sets its mark-up based on knowledge of the overall claim dollars being used in the final calculation, the outlier adjustment will still not result in an outlier payment that cover the drug cost. Use of the higher mark-up by Hospital B certainly results in a lower overall loss, but as the side-by-side comparison of CMS' outlier payment formula in the table below shows, both hospitals lose money on their CAR-T cases. It should also be noted that replacing the 10% marked-up CAR-T drug charge with the 400% marked-up charge would result in the claim's total charges increasing to $1,606,000 in our example.

Comparing Outlier Payments for Example Hospitals	Hospital A	Hospital B
Outlier Payment Calculation	10% Mark-up	400% Mark-up
Example MS-DRG 840 Base Payment	$ 16,736.00	$ 16,736.00
FY2018 Fixed Outlier Threshold	$ 26,713.00	$ 26,713.00
Example Hospital Operating CCR	0.2500	0.2500
Total Charges from Inpatient Claim	$ 524,300.00	$ 1,606,000.00
Calculated Hospital Cost (Charges * CCR)	$ 131,075.00	$ 401,500.00
Case Outlier Threshold (MS-DRG Pmt + Threshold)	$ 43,449.00	$ 43,449.00
Outlier Payment (Cost minus case threshold * 80%)	$ 70,100.80	$ 286,440.80
Total case payment (MS-DRG Payment Plus Outlier)	$ 86,836.80	$ 303,176.80

In summary, even the use of a 400% mark-up does not result in total case payment that covers the high CAR-T direct cost of $373,000. A financial loss of this magnitude for any individual case, much less multiple cases per year, is significant and will cause financial staff to question the facility's ability to provide this therapy to patients.

Inadequacy of New Technology Add-On Payment

If granted in FY2019, the NTAP should not be considered as a method to solve the reimbursement problems identified in this discussion. NTAP is capped at no more than 50 percent of the expected additional cost of the new technology, which means this formula is also dependent on the hospital's mark-up structure and will experience the same mark-up issues noted previously. In short, the NTAP carries the same risks for hospitals as the outlier formula. The example below compares Hospital A to Hospital B for estimated NTAP payments following

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CMS' existing formula and clearly shows the NTAP payment is insufficient to cover the invoice cost of the drug.

Comparing NTAP Payments for Example Hospitals	Hospital A	Hospital B
Example MS-DRG 840 Base Payment	$ 16,736.00	$ 16,736.00
Total Charges from Inpatient Claim	$ 524,300.00	$ 1,606,000.00
Example Hospital Operating CCR	0.25	0.25
Calculated Hospital Cost (Charges * CCR)	$ 131,075.00	$ 401,500.00
Less MS-DRG Payment ($131,075 minus $16,736)	$ 114,339.00	$ 384,764.00
Estimated CAR T NTAP Cap (Half of $373,000)	$ 186,500.00	$ 186,500.00
Estimated NTAP Payment	$ 114,339.00	$ 186,500.00
Hospital loss for invoice cost of CAR T	$ (258,661.00)	$ (186,500.00)

Future Rate-Setting for CAR-T beyond CMMI Demonstration

If CMS uses its authority to create separate payment for the product in the inpatient setting, we believe it will still need accurate data on both claims and in cost reports to support its demonstration project and to prevent significant charge compression problems. Furthermore, we believe it would be judicious for all parties if CMS plans to obtain the most accurate information on CAR-T patient care for use in its future rate-setting, even if separate payment for the product is being made under a CMMI model.

The following recommendations are offered as a "roadmap" for CMS to consider using in order to migrate back to the traditional rate-setting process at the end of the demonstration time period.

We believe there are four process steps required to obtain accurate data and prevent charge compression for high cost drugs and biologicals:

- Obtaining actual invoice expense and line item billed charge data for CAR-T on claims,
- Requesting a new dedicated revenue code series for CAR-T from NUBC,
- Creating new dedicated cost center for CAR-T, and
- Creating a new IPPS cost grouping for CAR-T, or cell and gene therapies, if CMS continues to use follow its current rate-setting methodology

We believe that the first of these processes – obtaining invoice expense and line item billed CAR-T charges on claims – should be implemented immediately under the CMMI authority as part of the demonstration we are requesting. We believe CMS needs to collect invoice cost information for CAR-T products through the duration of its CMMI demonstration so that it will have this data available at the earliest possible time, rather than planning to estimate CAR-T cost from billed charges. Obtaining this data from the outset would enable CMS to simultaneously provide accurate and fair reimbursement to hospitals providing this important new therapy to patients today under the CMMI authority, while also bypassing/avoiding the entire issue of

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charge compression under IPPS rate-setting in the future. We believe this methodology will be easy to implement for both providers and CMS alike as it uses components familiar to both currently for items like expensive blood clotting factors on inpatient claims. We believe the methodology we have outlined is simple and can easily be utilized to provide fair and appropriate reimbursement to both PPS and PPS-exempt hospitals despite the differences in reimbursement mechanics.

Implementation Timeframe

It is important to note that even if CMS concurs with all our suggestions and the components needed for future rate-setting, and also acts upon each one quickly, implementation will still take between 2-4 years and having data suitable for CMS's usual processes may take even longer. For example, a new revenue code series approved next year would be slotted for implementation around July 2019. Furthermore, adding a new cost center to expense reporting on hospital cost reports is not likely to appear until 2022 or 2023, at the earliest.

The expected delay in the use of established coding and billing pathways are part of why the use of CMMI's demonstration authority is so critical; it will provide immediate reimbursement relief to providers while laying the groundwork for more appropriate rate-setting in the future by CMS. It is during the immediate post-approval period that we believe CMS will need to obtain invoice cost data, switching to a more automated and integrated process over time.

If CMS acts immediately to collect both invoice cost and drug-specific charge information on claims either through the CMMI demonstration and/or through separate claims processing manual instructions to providers, CMS would have usable information for FY2019 rate-setting. CMS would be able to remove the CAR-T drug charge from claims and follow its usual MS-DRG rate-setting method for all remaining patient care charges reported on the claims. CMS would also be able to calculate the average CAR-T drug costs for the inpatient cases using invoice cost information. New MS-DRGs and associated relative weights could be established without the CAR-T drug cost and then CMS could either add back a separately calculated average CAR-T drug cost to create a relative weight inclusive of the product cost or could keep this piece separate and allow for a separate add-on payment until more data is collected. In either case, this method is intended to help avoid charge compression for these products in rate-setting until sufficient data is flowing into the newly designated revenue code and specific associated cost center in hospital cost reports.

We believe that this modified approach to MS-DRG rate-setting is fully defensible given the long-standing history of charge compression combined with the extraordinary expense of the CAR-T drug costs, coupled with the issue that these therapies are completely new and not incorporated into any existing hospital cost structures. For more details, please see separate attached letter regarding FY2019 MS-DRGs.

By CMS taking this "forward looking" approach, it would show the provider and patient communities that the Agency is sensitive not only to cost considerations, but to price transparency and patient access as it relates to these incredible new life-saving therapies.

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Summary and Contacts

We believe CMS has the authority, and a unique opportunity, to prevent significant financial strain to providers anxious to provide a new therapeutic option to a population with very few alternatives.

ASBMT welcomes the opportunity to discuss identified issues with the Agency. CAR-T is a transformative therapy for the field of oncology and ASBMT is committed to making it available to beneficiaries that may benefit and urge CMS to be a proactive partner in this endeavor. ASBMT peer-elected leaders, member clinicians and policy staff are available as a resource for CMS staff when issues associated with HCT, CAR-T and other cellular therapies are raised internally in the future. Please do not hesitate to reach out whenever we may be of assistance.

Krishna Komanduri, MD
ASBMT President, 2017-2018
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Appendix A

Claim Modifications for CAR-T Expense

CMS and hospitals prefer electronic claim transactions where all necessary information is provided directly on claims. To obtain CAR-T drug invoice cost on claims, we recommend that CMS will submit a formal request to the National Uniform Billing Committee (NUBC) for a unique value code for the hospital to report the actual invoice cost of CAR-T products on each applicable claim. Isolating the line item charge for the CAR-T product on the inpatient claim could be done by instructing hospitals to report the specific CAR-T product charge under revenue code 0636 as a separate line item on the UB-04 or 837I. This is the process CMS instructs hospitals to use to bill hemophilia blood clotting factors and would be familiar to many financial staff in these institutions.

This process would provide CMS all the needed elements directly on the claim to track CAR-T costs and isolate it for future rate-setting - that is, the invoice cost of CAR-T with the value code and the amount and the specific line item billed charge for the CAR-T product. Below is an illustration of what the claim would look like.

Example CAR T Inpatient Hospital Claim with Invoice Detail				
				FL04 = 0111
FL12 = Admit Date 10-1-17			FL17=Discharge Date 10-15-17	
	Value Code = xx		373,000.00	
FL 42 Revenue Code	FL 43 Description	FL 44 HCPCS	FL 46 Units	FL 47 Total Charges
0121	Room & Board		14	$ 49,000.00
0250	Pharmacy		100	$ 10,000.00
0270	Supplies		20	$ 1,500.00
0300	Laboratory		520	$ 50,000.00
0636	**Detailed Pharmacy**	**Jxxxx**	**1**	**$ 410,300.00**
0940	Other Tx Services		1	$ 3,500.00
0001	Total Charges			**$ 524,300.00**

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