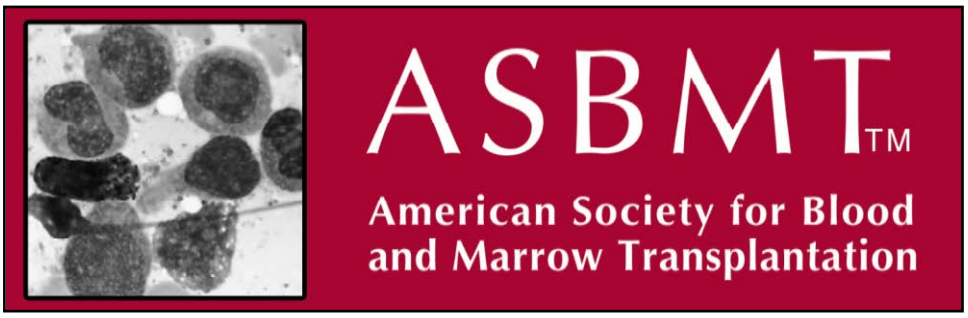

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April 7, 2017

ICD-10 Coordination and Maintenance Committee
Department of Health and Human Services
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850
ICDProcedureCodeRequest@cms.hhs.gov

Introduction

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 research, education, scholarly publication and clinical standards. ASBMT is dedicated to improving the application and success of blood and marrow transplantation by ensuring access to all patients who need hematopoietic cell transplants.

ASBMT appreciates the opportunity to comment on the ICD-10 coding proposal regarding Chimeric Antigen Receptor T Cell therapy (CAR-T) as exemplified by Kite Pharma's KTE-C19 (Axicabtagene Ciloleucel Cellular Immunotherapy). Our member physicians have extensive experience with the administration of cellular therapies for the purpose of treating hematologic malignancies. On November 30, 2016, CMS designated our physicians as a separate specialty for the purposes of performing hematopoietic cell transplantation and cellular therapies. Because of this clinical expertise, many of our member physicians will be actively engaged in the clinical administration of engineer T cell therapies such as CAR-T cells. The ASBMT will be monitoring and assessing the implications of all new coding proposals associated with CAR-T and other engineered T Cell therapies.

Clinical Overview

Patients being treated with KTE-C19 will have aggressive b-cell or follicular lymphomas that are refractory to previous treatment attempts. While these cases are diagnostically lymphomas, they resemble acute leukemia in terms of both their level of disease severity and the intensive need for physician monitoring and treatment of symptoms while curative intent therapies are administered. Other CAR-T cell products with different targets, such as acute lymphoblastic leukemia, will have resource consumption similar to the scenarios described in this comment letter. Prior to infusion of CAR-T cells, patients will receive cytoreductive chemotherapy

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designed to cause severe pancytopenia. Patients will need transfusions, prophylactic antibiotics and ongoing monitoring for unexpected complications. After the modified cells are infused, a subset of treated patients will experience adverse reactions related to the product, including an intensive immune system reaction known as cytokine release syndrome (CRS). CRS resembles sepsis in that it requires urgent intravenous fluid support, EKG and continuous monitoring through pulse oximetry. Patients will frequently need blood pressure support medications, antibiotics and, most critically, high doses of cloned immune modulators like interleukin 6. The higher risk of neurologic toxicity also requires these patients to have frequent neurologic examinations in addition to other critical care monitoring. Patients experiencing CRS will need to remain in the inpatient setting until symptoms resolve and they achieve blood cell count recovery.

At the 2017 American Academy for Cancer Research conference, Dr. Frederick Locke presented data showing that 13% of patients treated (N= 12) experienced Grade 3+ Cytokine Release Syndrome and 43% of patients (N=101) received tocilizumab (IL-6) during the ZUMA-1 study. 86% of the individuals participating in the trial had diagnoses of Stage III or IV disease and 70% had failed 3 or more previous therapies.[1] This data is supportive of ASBMT concerns that the episodes of care associated with the provision of Axi-Cel, and treatment for associated complications, will be resource intensive for the facility and the clinical team managing the patients.

ICD-10 Coordination and Maintenance Committee Documentation

In the agenda and materials supplied for the March 7-8, 2017 ICD-10 Coordination and Maintenance Committee (Committee) Meeting, CMS noted the following:

***Current Coding**: If desired, facilities can report intravenous infusion of KTE-C19 with one of the following ICD-10-PCS codes:*

3E03305 Introduction of Other Antineoplastic into Peripheral Vein, Percutaneous Approach
3E04305 Introduction of Other Antineoplastic into Central Vein, Percutaneous Approach

ASBMT Concerns with Current Coding

The perspective of the ASBMT is that the current coding advice provided by CMS does not adequately describe the care being provided. Additionally, the identified codes will not map to a

[1] Locke, F. AACR 2017 Plenary Session: *Immuno-oncology Biomarkers in Clinical Trials.* Abstract CT019; Sunday, April 2.

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specific DRG/MS-DRG, which will create later difficulties in identifying the costs and appropriate weight associated with the care episode. While we acknowledge that the latter issue is beyond the usual concerns of the Committee, we cannot discuss the issues in isolation.

While CMS notes that its Current Coding may be used by facilities "if desired", documentation from the ICD-10 Coordination and Maintenance will likely be interpreted by providers as directive guidance for the coding of the provision of KTE-C19 or other CAR-T products until the time of issuance of the requested new technology X code or, in the case of a denial of the new technology code request, indefinitely. The lack of a clear DRG/MS-DRG assignment will mean that these episodes of care will default to some of the lowest weighted DRGs, with assignment based on the other diagnostic codes submitted on the claim. As the providers of this care, we are very concerned that access to Seniors will be limited by inappropriately low reimbursement levels for a new, resource-intensive technology. The passage of the 2015 Medicare Access and CHIP Reauthorization Act (MACRA) and the establishment of the Quality Payment Program to monitor resource consumption associated with individual providers and/or facilities will create a situation in which providers will appear to be using resources far beyond the benchmark for other care episodes resulting the same DRG.

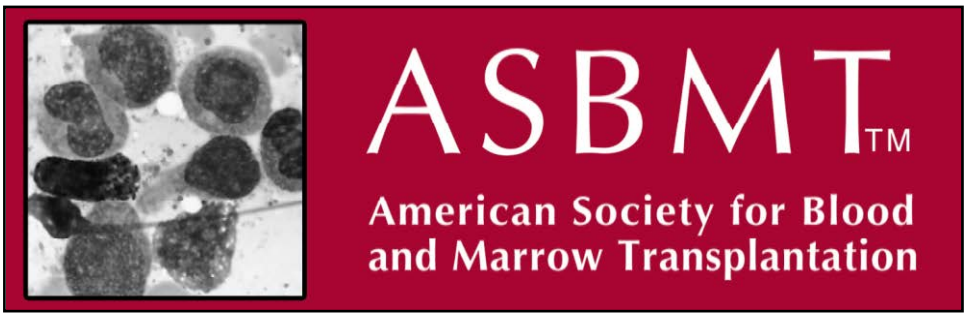
Recommended Alternative Interim Codes for Consideration

As an alternative, we suggest that the Committee consider utilizing the following codes as interim guidance for the coding of KTE-C19:

3E03302 Introduction of high-dose interleukin-2 into peripheral vein, percutaneous approach
3E04302 Introduction of high-dose interleukin-2 into central vein, percutaneous approach

Rationale for Suggested Alternative

Codes 3E03302/3E03302 (Alternative Codes) are ICD-10-PCS codes, which describe the extended use of high-dosages of interleukin-2 for antineoplastic clinical purposes. The Alternative Codes map to MS-DRG 837 (Chemotherapy with Acute Leukemia as Secondary Diagnosis or with High Dose Chemotherapeutic Agent with MCC) and MS-DRG 838 (Chemotherapy with Acute Leukemia as Secondary Diagnosis with CC or High Dose Chemotherapeutic Agent), respectively. MS-DRGs 837/838 are DRGs which are clinically appropriate to the treatment being provided when utilizing KTE-C19 and also reflect the resource use during these episodes of care.



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The complexity of the inpatient admission that utilizes KTE-C19 requires rigorous patient oversight involving Intensive Care Medicine and Cardiopulmonary specialists in addition to the primary Hematopoietic Cell Transplant/Cellular Therapy physician and/or Hematology/Oncology physician. In the event of a post-infusion complication or an adverse event, as a significant number of patients will face (noted earlier in our commentary), the managing physician will prescribe use of tocilizumab, an antibody against the IL6-receptor, to counteract Cytokine Release Syndrome. Patients that experience CRS and receive the administration of tocilizumab will require even greater resource utilization, which may include a significantly longer hospital stay and additional nursing support, as compared to conventional chemotherapy. While not all individuals receiving CAR-T cell therapy like KTE-C19 will need tocilizumab, each patient will need to be monitored more closely and supported by the facility until it becomes clear that the potential need for this therapeutic intervention has passed.

The use of the suggested Alternative Codes allows CMS to have a mechanism for capturing the cost of care for CAR-T cell therapy such as KTE-C19, while it assesses the best long-term coding and reimbursement solution. Alternatively, use of the Current Coding, as identified in the Committee's documents, will not allow for the tracking of these care episodes and will result in inappropriately low payment rates.

CMS Precedent for Inclusion of High-Dose Interleukin Treatment in MS-DRG 837/838

As is described in the following excerpt from the Inpatient Prospective Payment System Fiscal Year 2008 Final Rule, CMS acknowledges this same issue during the early use of HD-IL-2 and clarifies that antineoplastic care episodes utilizing HD-IL-2 should be assigned to a MS-DRG more reflective of the resources utilized during the provision of care.

DEPARTMENT OF HEALTH AND HUMAN SERVICES Centers for Medicare & Medicaid Services 42 CFR Parts 411, 412, 413, and 489 [CMS-1533-FC] RIN 0938-AO70 Medicare Program; Changes to the Hospital Inpatient Prospective Payment Systems and Fiscal Year 2008 Rates https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/downloads/CMS-1533-FC.pdf

Administration of high-dose Interleukin-2 (HD-IL-2) is a hospital inpatient-based regimen that can produce durable remissions of metastatic renal cell cancer and metastatic melanoma in a subset of patients. In contrast to traditional cytotoxic chemotherapies which target cancer cells directly, HD-IL-2 enhances the body's natural cancer defenses by stimulating the growth and

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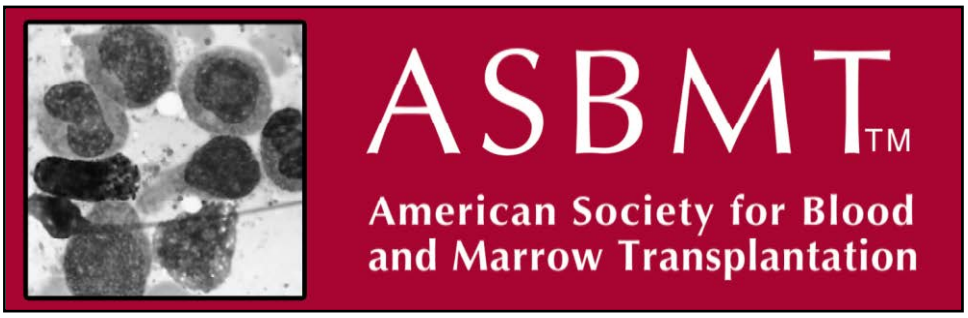
activity of cancer-killing white blood cells. HD-IL-2 therapy is associated with severe complications that can include: hypotension, metabolic acidosis, acute renal failure, arrhythmia, myocardial inflammation, coagulation defects, hyperthyroidism, psychosis, respiratory distress syndrome, catheter related septicemia, hyperbilirubinemia and thrombocytopenia. To safely administer HD-IL-2, the FDA-approved label states that HD-IL-2 "should be administered in a hospital setting under the supervision of a qualified physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available." Strict nursing protocols must be followed in order to minimize adverse events such as cardiac arrhythmias as well as severe hypotension. Because it is associated with such severe side effects, HD-IL-2 therapy requires substantially greater resource utilization, including longer hospital stays and additional nursing support, than conventional chemotherapy. Conventional chemotherapy may be administered to patients either on an outpatient basis or through a series of short (that is, 1 to 3 day) inpatient stays.

In spite of the possibility of erroneous coding of low-dose IL-2 cases to procedure code 00.15 instead of the more appropriate code 99.28 as discussed above, the data do not currently suggest a problem with Medicare payment for most of the HD-IL-2 cases assigned to MS-DRGs 837, 838, and 839. However, the data do suggest that the costs of cases of IL-2 coded with 00.15 currently assigned to MS-DRG 839 are closer to MS-DRG 838. Therefore, for FY 2008, we are assigning procedure code 00.15 (High-dose infusion of Interleukin-2 (IL-2)) to MS-DRG 837 (Chemotherapy with Acute Leukemia as Secondary Diagnosis or with High Dose Chemotherapeutic Agent with MCC) and MS-DRG 838 (Chemotherapy with Acute Leukemia as Secondary Diagnosis with CC or High Dose Chemotherapeutic Agent).

Conclusion

ASBMT acknowledges that the ICD-10-PCS description of HD-IL-2 is an accurate clinical reflection of that particular service and that the assignment of HD-IL-2 to MS-DRGs 837/838 was put in place due to actual and on-going reimbursement concerns, versus our request for the use of a code that is not a clear description of the service based on our anticipated issues. ASBMT is currently planning to submit requests to the Committee later in 2017 that would update the ICD-10-PCS Transfusion Section (Table 302) with Substances that reflect the true clinical nature of the cells being administered during the infusion of Chimeric Antigen Receptor T-Cell or other engineered T Cell therapies. The use of the suggested Alternative Codes would



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serve as an interim descriptor and coding solution that would allow CMS to track and monitor the resource utilization associated with a new class of therapeutic agents.

The ASBMT appreciates the opportunity to offer information and guidance in advance of the Committee's final determination about the appropriate coding for KTE-C19. We welcome future discussion with CMS on this issue. Please contact Stephanie Farnia, Director, Health Policy at StephanieFarnia@asbmt.org with any questions. Dr. James Gajewski, MD, MACP, (jlgajewski@yahoo.com) can answer any additional questions related to the impact of coding on physician resource use metrics.

Sincerely,

AMERICAN SOCIETY FOR BLOOD & MARROW TRANSPLANTATION

Krishna Komanduri, MD
President, 2017-2018