PERSONALIZED MEDICINE COALITION

June 25, 2018

Seema Verma
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Avenue, SW
Washington, DC 20201

Sent electronically

RE: Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2019 Rates; Proposed Quality Reporting Requirements for Specific Providers; Proposed Medicare and Medicaid Electronic Health Record (EHR) Incentive Programs (Promoting Interoperability Programs) Requirements for Eligible Hospitals, Critical Access Hospitals, and Eligible Professionals; Medicare Cost Reporting Requirements; and Physician Certification and Recertification of Claims [CMS-1694-P]

Dear Administrator Verma:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 230 institutions across the health care spectrum, appreciates the opportunity to submit comments regarding the Centers for Medicare & Medicaid Services (CMS)' Medicare Hospital Inpatient Prospective Payment System (IPPS) Proposed Rule for FY 2019.[i] While we recognize there are numerous important payment issues addressed in the proposed rule, PMC's comments are confined to the impact of specific proposed payment changes on beneficiary access to U.S. Food and Drug Administration (FDA)-approved CAR T-cell therapies and other significant cell and gene therapies like them in the future. PMC commends CMS for its efforts to ensure appropriate reimbursement and rate setting for CAR T-cell therapies through proposed updates for FY 2019, however we suggest additional considerations below that may lead CMS to the creation of a long-term solution for adequate payment of these highly specialized medicines.

Personalized medicine is an evolving field that uses diagnostic tools to identify specific biological markers, often genetic, to help determine which medical treatments and procedures will be best for each patient. By combining this information with an individual's medical history, circumstances, and values, personalized medicine allows doctors and patients to develop targeted prevention and treatment plans.

Personalized medicine is helping to shift the patient and provider experience away from trial-and-error and toward a more streamlined process for making clinical decisions, which will lead to improved patient outcomes, a reduction in unnecessary treatment costs, and better patient and provider satisfaction. As noted above, PMC's members are leading the way in personalized medicine and recommend that patients who may benefit from this approach undergo appropriate testing and tailored treatment as soon as possible during their clinical experiences.

PMC recently released *Personalized Medicine at FDA: 2017 Progress Report.* The report documents a record number of new personalized medicine approvals by FDA. This marks the fourth consecutive year that personalized medicines accounted for more than 20 percent of all new drug approvals.[ii] Two of the 19 personalized medicines approved in 2017 were CAR T-cell therapies, an adoptive cell transfer (ACT) class of immunotherapies whereby a patients' immune cells are collected and genetically changed to treat cancer. Because of its potential to further transform cancer care for patients with incurable blood cancers, the American Society of Clinical Oncology named ACT using CAR T-cells their 2018 "Advance of the Year." [iii]

CAR T-cell therapy is the result of decades of research in biology, genetics, and immunology supported by the U.S. National Institutes of Health and the biopharmaceutical industry. Fortunately for patients, the pipeline for significant cell and gene therapies is robust. A study conducted by the Massachusetts Institute of Technology NEWDIGS FoCUS Project predicts that by the end of 2022 there will be about 40 gene therapy products approved by the FDA, with 45 percent of these for products targeting cancer.[iv] In light of this entirely new approach to treatment, FDA has developed new structures for evaluating cell and gene therapies and has demonstrated remarkable speed in bringing CAR T-cell therapies to market. Like FDA, CMS has signaled a belief that CAR T-cell therapies represent a significant advancement in cancer care for specific patient populations, and we appreciate the opportunity to provide feedback on how CMS can continue to provide beneficiary access to these and other life-saving cell and gene therapies.

Statement of Neutrality

Many of PMC's members will present their own responses to CMS and will actively advocate for those positions. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance, and are not intended to impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to the Medicare IPPS Proposed Rule for FY 2019.

Burden of Disease and Treatment with CAR T-cell Therapies

The two CAR T-cell therapies approved by FDA in 2017 are intended to treat children and young adults with acute lymphoblastic leukemia (ALL) and adults with diffuse large B-cell lymphoma (DLBCL). ALL and DLBCL are cancers with very poor prognoses. The expected survival for adults with relapsed ALL is less than six months. Among children with cancer, relapsed ALL is a leading cause of cancer-related death.[v] Treatment with CAR T-cell therapy for ALL resulted in complete remissions in up to 90 percent of adults and children with this disease. In some patients, remissions have lasted up to two years. Such durable remissions offered many patients the chance to undergo curative bone marrow transplants.[vi]

DLBCL is the most common type of non-Hodgkin lymphoma. In a multi-center clinical trial of patients with DLBCL that worsened after at least two prior therapies, the cancer responded to a CAR T-cell therapy called tisagenlecleucel in 59 percent of 51 patients, and the cancer went into remission in 43 percent of patients. At 6 months, 79 percent of patients had not had a recurrence of lymphoma. In a different clinical trial, patients with relapsed or refractory DLBCL, refractory primary mediastinal B-cell lymphoma, or transformed follicular lymphoma, received another CAR T-cell therapy, axicabtagene ciloleucel. Among the first 92 patients who were treated, the response rate was 82 percent, with complete remissions occurring in 54 percent of patients.[vii]

CAR T-cell therapies have had a profound impact in extending the lives of some patients with ALL and DLBCL. Researchers are now pursuing CAR T-cell therapies in other types of cancer with promising results. For example, an early clinical trial of patients with relapsed, treatment resistant multiple myeloma reported that 33 out of 35 (94 percent) patients demonstrated clinical remission upon receiving a CAR T-cell therapy targeting B-cell maturation protein.[viii] We expect that innovation in cell and gene therapies will continue providing clinical advances for small patient populations and resulting in similar durable health outcomes.

Challenges with Current Reimbursement Paradigm

Tremendous advancement in CAR T-cell treatment should be supported by a thoughtful reimbursement structure. PMC is committed to ensuring that coverage and reimbursement policies do not serve as a barrier to the timely and appropriate use of personalized treatment options by providers. In the Medicare IPPS Proposed Rule for FY 2019, CMS acknowledges some of the same unique challenges we have observed in relation to CAR T-cell therapies and the current reimbursement paradigm.

Diagnosis Related Group (DRG) payments are set with a two-year lag, so new technologies are often not included in payment calculations due to CMS' use of historical costs and charges. As a result, for a period of time, hospitals are not fully reimbursed for the use of innovative technologies. In the case of CAR T-cell therapies, hospitals can be left with more than $200,000 in unreimbursed costs for patient care.

Limited options are available for additional payment to DRGs. The New Technology Add-On Payment (NTAP) program used by CMS to provide additional payment for breakthrough technologies was not developed with CAR T-cell therapies and the small patient populations they serve in mind. They cannot be adequately applied and they expire after a few years. Even with an NTAP, hospitals still require a way to recover the costs of CAR T-cell therapies in the short term and in the long term, after they are no longer eligible for NTAP payments.

PMC appreciates that CMS has proposed payment updates to the current inpatient payment structure to continue access to CAR T-cell therapies and that the agency remains open to stakeholder feedback on how the reimbursement paradigm can be structured in the future to ensure sufficient reimbursement for coverage of cell and gene therapies.

Considerations for CMS in Finalizing Proposed Changes

The Medicare IPPS Proposed Rule for FY 2019 signals a willingness to adapt the current reimbursement structure to account for innovative treatments and proposes payment updates to the current inpatient payment structure that would continue access to CAR T-cell therapies. PMC is pleased with the proposals put forward by CMS but asks the agency's consideration of the following issues:

- CAR T-cell therapies are breakthrough products for patients that are worthy of an NTAP payment to assist hospitals. Establishing an NTAP is commendable, but a payment of 50 percent is not sufficient to make hospitals whole. CMS has the regulatory authority to increase the NTAP amount and we would encourage you to do so in future years.

- In the IPPS Proposed Rule, CMS raises the possibility of using a Cost to Charge Ratio of 1.0 so that hospital charges for CAR T-cell treatment would be fully reflected in rate-setting, NTAP, and outlier calculation. PMC generally supports this proposal because it could significantly mitigate hospital losses but, we would note that they may still be left with a loss of more than $25,000 per case.

- Prior to the IPPS Proposed Rule, the expectation was that CAR T-cell cases would be assigned to MS-DRGs for Lymphoma & non-acute leukemia with MCC with a reimbursement of approximately $20,000. CMS has proposed in the Rule to map CAR T-cell cases to a higher paying alternative for Autologous Bone Marrow Transplant w/CC/MCC. While the increased reimbursement rate of $39,000 is a welcome improvement, it does not come close to the full cost of the therapy. Over the long-term, this approach may continue to present access barriers for patients. PMC suggests that CMS consider the option of including CAR T-cell cases in the MS-DRG for Autologous Bone Marrow Transplant w/CC/MCC and then paying for the drug separately at its Average Sales Price (ASP) as a bridge to a longer-term sustainable solution.

- The IPPS Proposed Rule notes the possible creation of an alternative MS-DRG for CAR T-cell therapies that could take into account an appropriate portion of the ASP for these drugs. A CAR T-cell specific MS-DRG could eliminate the need for NTAP payments and help make hospitals whole depending on how CMS defines an appropriate portion of a CAR T-cell therapy's ASP. PMC supports further exploration of this alternative. The creation of a new MS-DRG can provide stability for both providers and patients over the long-term by setting a new rate. PMC understands that there are technical challenges in setting a rate that provides adequate payment across the range of Medicare providers. We urge CMS to continue to work with stakeholders to incorporate the appropriate amount of CAR T-cell therapy costs into the new MS-DRG calculation to ensure appropriate reimbursement for providers.

The potential changes in the IPPS Proposed Rule will significantly impact current FDA-approved CAR T-cell therapies and lay the foundation for a reimbursement pathway that will affect these and other novel cell and gene therapies. PMC encourages CMS to adopt a pathway that creates flexibility in the adoption of future innovations into the IPPS reimbursement

structure, enables providers and patients to select the most appropriate treatment and site of care, and allows for continued refinement by all stakeholders to improve patient outcomes while appropriately managing costs.

Conclusion

Thank you for your leadership and for considering our comments. As CMS moves forward with finalizing the Medicare IPPS Rule for FY 2019, we urge you to ensure that the decisions made bring us closer to the goal PMC shares with the agency of delivering appropriate, efficient, and accessible health care to every patient. We welcome the opportunity to serve as a resource for you. If you have any questions about the content of this letter, please contact me at 202-589-1769 or cbens@personalizedmedicinecoalition.org.

Sincerely,

Cynthia A. Bens
Senior Vice President, Public Policy

---

[i] Centers for Medicare & Medicaid Services. *Medicare Program; Hospital Inpatient Prospective Payment Systems for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2019 Rates; Proposed Quality Reporting Requirements for Specific Providers; Proposed Medicare and Medicaid Electronic Health Record (EHR) Incentive Programs (Promoting Interoperability Programs) Requirements for Eligible Hospitals, Critical Access Hospitals, and Eligible Professionals; Medicare Cost Reporting Requirements; and Physician Certification and Recertification of Claims*. April 22, 2018 https://s3.amazonaws.com/public-inspection.federalregister.gov/2018-08705.pdf

[ii] Personalized Medicine Coalition. *Personalized Medicine at FDA 2017 Progress Report*. January 30, 2018 http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_2017_Progress_Report.pdf

[iii] American Society of Clinical Oncology. *Clinical Cancer Advances of 2018*. January 30, 2018 https://www.asco.org/sites/new-www.asco.org/files/content-files/research-and-progress/documents/CCA-2018-Report.pdf

[iv] Massachusetts Institute of Technology NEWDIGS FoCUS Project. *Existing Gene Therapy Pipeline Likely to Yield Dozens of Approved Products Within Five Years; Research Brief.* November 13, 2017. http://newdigs.mit.edu/sites/default/files/FoCUS_Research_Brief_2017F211v011.pdf

[v] American Society of Clinical Oncology. *At the Leading Edge of Precision Medicine: Souped-up Immune Cell.* April 5, 2017. https://www.asco.org/about-asco/press-center/cancer-perspectives/leading-edge-precision-medicine-souped-immune-cells

[vi] American Society of Clinical Oncology. *At the Leading Edge of Precision Medicine: Souped-up Immune Cell.* April 5, 2017. https://www.asco.org/about-asco/press-center/cancer-perspectives/leading-edge-precision-medicine-souped-immune-cells

[vii] American Society of Clinical Oncology. *Clinical Cancer Advances of 2018*. January 30, 2018 https://www.asco.org/sites/new-www.asco.org/files/content-files/research-and-progress/documents/CCA-2018-Report.pdf

[viii] Frank (Xiaohu) Fan, Wanhong Zhao, Jie Liu, Aili He, Yinxia Chen, Xingmei Cao, Nan Yang, Baiyan Wang, Pengyu Zhang, Yilin Zhang, Fangxia Wang, Bo Lei, Liufang Gu, Xugeng Wang, Qiuchuan Zhuang, Wanggang Zhang; Nanjing Legend Biotech, Nanjing, China; Hematology, The Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China. *Durable Remissions with BCMA Specific Chimeric Antigen Receptor (CAR)-modified T Cells in Patients with Refractory/Relapsed Multiple Myeloma.* June 5, 2017. https://meetinglibrary.asco.org/record/153928/abstract