

June 25, 2021

Chiquita Brooks-LaSure
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
Hubert H. Humphrey Building, Room 445-G
200 Independence Avenue SW
Washington, DC 20201

RE: File code CMS-1752-P

Dear Ms. Brooks-LaSure:

The Medicare Payment Advisory Commission (MedPAC) welcomes the opportunity to comment on the Center for Medicare and Medicaid Services' (CMS's) proposed rule entitled "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 2022 Rates; Quality Programs and Medicare Promoting Interoperability Program Requirements for Eligible Hospitals and Critical Access Hospitals; Proposed Changes to Medicaid Provider Enrollment; and Proposed Changes to the Medicare Shared Savings Program," *Federal Register* 86, no. 88, pp. 25070–25790 (May 10, 2021). We appreciate CMS's ongoing efforts to administer and improve Medicare's payment systems for hospitals, particularly given the many competing demands on the agency's staff.

In this letter we comment on proposals to:

- Use 2019 data instead of 2020 data for ratesetting in both the hospital inpatient prospective payment system (IPPS) and long-term care hospital (LTCH) PPS
- Repeal the plan to use "market-based" data to set Medicare severity–diagnosis related group (MS–DRG) relative weights
- Change rural reclassification cancellation requirements

We also comment on several issues related to chimeric antigen receptor T-cell (CAR-T) technologies, including applications for new technology add-on payments and the need for CMS to ensure appropriate use and collect evidence on the effectiveness of these products.

Use 2019 data for fiscal year 2022 IPPS and LTCH PPS ratesetting

For fiscal year (FY) 2022 ratesetting, CMS typically would use the FY 2020 Medicare Provider Analysis and Review (MedPAR) file and the FY 2019 Healthcare Cost Report Information System (HCRIS) dataset, which consists of all cost reports beginning in FY 2019, including those that end in FY 2020. However, both sources (collectively referred to as FY 2020 data) reflect utilization and costs of inpatient services affected by the coronavirus public health emergency (PHE). Specifically, FY 2020 data reflect increases in patients seeking care for coronavirus disease 2019 (COVID-19)-related and other respiratory illnesses, patients deferring and delaying non-COVID-19-related care during the PHE, and increased growth in estimated real case mix. With the vaccine for COVID-19 available in 2021 and beyond, these conditions are unlikely to persist into FY 2022. Therefore, CMS proposes to use FY 2019 data for setting FY 2022 rates, asserting that the FY 2019 data will provide a better overall approximation of FY 2022 and yield more accurate relative weights and outlier fixed-loss amounts than FY 2020 data.

Comment

The Commission appreciates the challenge CMS faces in setting rates for FY 2022, particularly in determining which data, FY 2019 or FY 2020, are most likely to approximate FY 2022. While the Commission supports CMS's long-standing practice of using the most recent full fiscal year of data to update the IPPS and LTCH PPSs, given the effects of the PHE on acute care and long-term care hospitals' utilization and costs in FY 2020 and widespread availability of COVID-19 vaccination starting in 2021, we concur that FY 2022 cases will likely more closely resemble 2019 cases than 2020 cases. Therefore, we support CMS's proposal to use FY 2019 MedPAR and FY 2018 HCRIS files in setting FY 2022 rates.¹

Repeal of the plan to use "market-based" data to set Medicare MS-DRG weights

MS-DRG weights are used to set a relative payment rate for each MS-DRG that is proportionate to the average cost of care of cases assigned to the MS-DRG. For example, if hospitals' costs per discharge for patients with MS-DRG A are (on average) twice the costs for MS-DRG B, CMS will try to set the payment weight for MS-DRG A equal to twice the payment weight for MS-DRG B. MS-DRG weights that are too low or too high relative to costs are inequitable and create incentives for providers to expand service lines that are overpaid and reduce service lines that are underpaid. Currently, MS-DRG weights are set using the estimated relative costs of different MS-DRGs based on hospital cost report data.

¹ In instances where we have expressed support for using FY 2020 data to set FY 2022 rates, as we did in our recent comment on CMS's proposed rule for setting FY 2022 rates for inpatient rehabilitation facilities (IRFs), other factors also influenced that support—specifically, the need to use data reflecting changes to the IRF case-mix group definitions that were implemented in FY 2020 and will continue to be used in FY 2022.

In the IPPS final rule for FY 2021, CMS stated that it would shift to using “market-based” MS–DRG weights beginning in 2024.² These weights would be computed using relative rates paid by Medicare Advantage (MA) plans for different MS–DRGs. For example, if hospitals’ median MA payment rate for cardiac bypass without complications or comorbidities (CCs) was three times the median MA rate for pneumonia without CCs, then the MS–DRG weight for cardiac bypass would be set at three times that for pneumonia.

In a reversal of last year’s final rule, CMS is now proposing to not use MA plans’ price data to set fee-for service (FFS) relative weights in 2024 or any future years.

Comment

In our comments on the FY 2021 proposed rule, we opposed CMS’s plan to use MA rates to set FFS rates.³ We noted that MA plans almost always explicitly use Medicare FFS relative weights to set their payment rates.⁴ Therefore, using MA plans’ rates to set FFS MS–DRG weights would be circular and would not bring true market-based payment rates into the Medicare hospital rate-setting process. Consistent with our opposition to the FY 2021 proposal to use “market-based” data to set Medicare MS–DRG weights (which was later finalized), we support CMS’s current proposal to repeal this plan.

Change rural reclassification cancellation requirements

Under section 1886(d)(8)(E) of the Social Security Act and §412.103 of the Medicare regulations, a qualifying hospital geographically located in an urban area may reclassify as rural for payment purposes. A hospital will retain its rural status under §412.103 without need for approval until there is a change in the circumstances under which the classification was approved or the hospital chooses to cancel its reclassification. A hospital with an urban-to-rural reclassification under §412.103 receives a wage index reflective of its reclassified rural area, instead of the urban area in which it is geographically located. A state’s rural wage index is inclusive of wage data of both hospitals located in a rural area and those that reclassify into the rural area, with some exceptions. This wage index value is used to determine a hospital’s base Medicare payments under the IPPS. In order to include the wage data of reclassified hospitals in calculations of the rural wage index

² Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2020. Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and final policy changes and fiscal year 2021 rates; quality reporting and Medicare and Medicaid Promoting Interoperability Programs requirements for eligible hospitals and critical access hospitals. Final rule. *Federal Register* 85, no. 182 (September 18): 58432–59107.

³ Medicare Payment Advisory Commission. 2020. Comment letter on CMS’s proposed rule entitled “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 2021 Rates; Proposed Quality Reporting Requirements for Specific Providers; Medicare and Medicaid Promoting Interoperability Programs Proposed Requirements for Eligible Hospitals and Critical Access Hospitals; Proposed Rule.” July 7.

⁴ Berenson, R. A., J. H. Sunshine, D. Helms, et al. 2015. Why Medicare Advantage plans pay hospitals traditional Medicare prices. *Health Affairs* 34, no. 8 (August): 1289–1295. (While the Berenson study is six years old, our recent examination of 2020 data from a sample of hospitals disclosing prices received from MA plans support Berenson’s findings that MA plans often set rates equal to 100 percent of FFS rates.)

value, CMS instituted a lock-in date by which hospitals seeking reclassification under §412.103 must submit their applications.⁵

In the FY 2020 IPPS/LTCH PPS final rule, CMS noted that hospitals with relatively low wage index values could time their §412.103 applications so that they are approved after the lock-in date. Because the wage data of hospitals that reclassify after the lock-in date are not included in the calculation of the rural wage index, these hospitals would receive a reclassified wage index that is higher than it would have been had their data been included. In the next fiscal year, these hospitals could cancel their rural reclassifications prior to the lock-in date and then reapply again after the lock-in date, such that they could continue to receive a wage index that was not inclusive of their wage data. CMS estimates this manipulation of the rural reclassification process resulted in the rural wage index of one state to increase by 4 percent between the FY 2020 proposed and final rules, and the increase could have been up to 10 percent in certain states. CMS said the agency would monitor the situation and determine if necessary action should be taken in future rulemaking.⁶

In the FY 2021 IPPS/LTCH PPS final rule, CMS found certain hospitals were indeed timing their rural reclassifications, cancellations, and re-applications under §412.103 to obtain higher wage index values. For example, in one state, five hospitals with wage data that would have lowered their state's rural wage index requested to cancel their §412.103 rural reclassifications for FY 2021. These five hospitals then reapplied and were approved for rural reclassification, essentially receiving a higher wage index without having their own data included in the wage index calculation.⁷

For FY 2022, CMS proposes to require that requests to cancel rural reclassification be submitted no earlier than one calendar year after the reclassification effective date. CMS also proposes to make a hospital's cancellation of its rural reclassification status effective for "the Federal fiscal year that begins in the calendar year after the calendar year in which the cancellation request is submitted." For example, under the CMS proposal, a cancellation request submitted on December 31, 2021

⁵Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2016. Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and policy changes and fiscal year 2017 rates; quality reporting requirements for specific providers; graduate medical education; hospital notification procedures applicable to beneficiaries receiving observation services; technical changes relating to costs to organizations and Medicare cost reports; finalization of interim final rules with comment period on LTCH PPS payments for severe wounds, modifications of limitations on redesignation by the Medicare Geographic Classification Review Board, and extensions of payments to MDHs and low-volume hospitals. Final rule. *Federal Register* 81, no. 162 (August 22): 56931–56932.

⁶Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2019. Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and policy changes and fiscal year 2020 rates; quality reporting requirements for specific providers; Medicare and Medicaid Promoting Interoperability Programs requirements for eligible hospitals and critical access hospitals. Final rule. *Federal Register* 84, no. 159 (August 16): 42044–42701.

⁷Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2020. Medicare program; hospital inpatient prospective payment systems for acute care hospitals and the long-term care hospital prospective payment system and final policy changes and fiscal year 2021 rates; quality reporting and Medicare and Medicaid Promoting Interoperability Programs requirements for eligible hospitals and critical access hospitals. Final rule. *Federal Register* 85, no. 182 (September 18): 58432–59107.

would be effective October 1, 2022; but a cancellation request submitted on January 1, 2022 would not become effective until October 1, 2023. These proposed changes aim to ensure a hospital that is reclassified to rural will have its data included in the calculation of the rural wage index for at least one federal fiscal year before its rural status can be canceled.

Comment

The Commission supports the implementation of these proposed policy changes to reduce inappropriate manipulation of the rural reclassification process at §412.103. We agree with CMS that the practice of applying for and canceling rural reclassification to manipulate a state's rural wage index is detrimental to the stability and accuracy of the Medicare wage index system. The Commission also reiterates its June 2007 recommendations on wage index reform.⁸ We recommended that the Congress repeal the existing hospital wage index and instead implement a market-level wage index for use across the IPPS and other PPSs, including certain post-acute care providers. Specifically, our recommended wage index system would:

- use wage data from all employers and industry-specific occupational weights,
- adjust for geographic differences in the ratio of benefits to wages,
- adjust at the county level and smooth large differences between counties, and
- include a transition period to mitigate large changes in wage index values.

Compared with the current system, the wage index system we proposed would more fully reflect input prices, automatically adjust for occupational mix, reduce circularity, and reduce large differences between adjoining areas. Two significant research evaluations commissioned by the Secretary concluded that MedPAC's proposed wage index system would be an improvement over Medicare's current hospital wage index system.^{9,10} We understand that eliminating the current wage index system and the associated apparatus (such as the rural floors and reclassifications) would require congressional action, but we urge the agency to consider our recommendations and make adjustments to the current system where it has the authority to do so. In particular, the continued increase in the number of IPPS hospitals applying for and being granted geographic reclassifications underscores the need to fix flaws in current wage index policy in a more uniform and consistent manner.

⁸ Medicare Payment Advisory Commission. 2007. *Report to the Congress: Promoting greater efficiency in Medicare*. Washington, DC: MedPAC.

⁹ Institute of Medicine. 2011. *Geographic adjustment in Medicare payment, Phase I: Improving accuracy*. Second edition. Washington, DC: The National Academies Press.

¹⁰ MaCurdy, T, T. DeLeire, K. Lopez de Nava. et al. 2009. *Revision of Medicare wage index. Final report, Part I*. MaCurdy, T, T. DeLeire, K. Lopez de Nava. et al. 2010. *Revision of Medicare wage index. Final report, Part II*. <https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Wage-Index-Files-Items/CMS1237065.html>.

NTAP and other policy issues related to CAR-T

The FY 2022 proposed rule discusses applications by four manufacturers of new CAR-T therapies seeking IPPS new technology add-on payments (NTAPs) for hospital discharges when these products are provided. CAR-T is a type of immunotherapy used to treat certain types of cancer that involves collecting and genetically modifying the patient's own T-cells. Specifically, manufacturers have applied for an IPPS NTAP in FY 2022 for:

- Tecartus for adult patients with relapsed or refractory mantle cell lymphoma, approved by the Food and Drug Administration (FDA) in July 2020;
- Breyanzi for adult patients with relapsed or refractory large B-cell lymphoma who have already tried two or more other treatments, approved by the FDA in February 2021;
- Abecma for adult patients with relapsed or refractory multiple myeloma who have already tried four or more other treatments, approved by the FDA in March 2021; and
- Ciltacabtagene autoleucel for previously treated patients with relapsed or refractory multiple myeloma, not yet approved by the FDA.

The NTAP policy provides additional payments for inpatient admissions with relatively high costs involving eligible new medical services or technologies, while preserving some of the incentives inherent under an average-based prospective payment system. CMS evaluates applications for an NTAP submitted by manufacturers based on three criteria: (1) the service or technology must be new,¹¹ (2) the service or technology must demonstrate a substantial clinical improvement over existing services or technologies,¹² and (3) the cost of the technology must exceed MS-DRG-specific thresholds. For cases involving eligible new technologies, NTAPs are generally set at 65 percent of the lesser of (1) the costs of the new technologies (i.e., manufacturer's price) or (2) the amount by which the cost of the case exceeds the otherwise applicable IPPS operating payment (including indirect medical education and disproportionate share payments).

Medicare has covered and paid for CAR-T therapies since the first two products, Kymriah and Yescarta, were launched in the U.S. in FY 2018 to treat adult patients with certain advanced lymphomas (who have already tried two other kinds of treatment).¹³ CAR-T products are extremely high-priced. For example, based on publicly available payment rate information for CAR-T products under the outpatient prospective payment system in effect as of January 2021, the average sales prices of Yescarta and Kymriah appear to be approximately \$373,000 and \$401,000,

¹¹ CMS does not consider a technology "new" for the purposes of receiving an NTAP after CMS has recalibrated the MS-DRGs based on available data to reflect the technology's cost. An NTAP designation lasts no more than two to three years for a given technology.

¹² In addition, certain transformative new devices and antimicrobial products may qualify under an alternative inpatient new technology add-on payment pathway, as set forth in the regulations at §412.87(c) and (d).

¹³ Kymriah is also approved for young patients (up to age 25) with certain acute lymphocytic leukemias.

respectively.¹⁴ The list prices of the CAR-Ts that CMS is considering for an NTAP in FY 2022 range from \$373,000 to approximately \$420,000.¹⁵

CMS's inpatient payment policies for CAR-Ts have evolved. Initially, Medicare paid IPPS hospitals for CAR-T therapies under MS-DRG 016, which grouped together patients receiving certain bone marrow transplants and patients receiving Kymriah and Yescarta. For admissions during FYs 2019 and 2020, CMS paid an NTAP for these CAR-Ts. Hospitals could also receive outlier payments for patients receiving CAR-T therapy, set at 80 percent of the amount by which the estimated cost of the case exceeds Medicare's payment after a fixed-loss amount has been reached. Beginning in fiscal year 2021, CMS created MS-DRG 018 (Chimeric Antigen Receptor (CAR) T-cell Immunotherapy) for cases that furnish CAR-Ts, including Kymriah and Yescarta (reported using ICD-10-PCS procedure codes XW033C3 or XW043C3). It is expected that the new CAR-Ts that CMS is considering for an NTAP payment would be paid for under this MS-DRG.¹⁶ The MS-DRG for CAR-T has the highest base payment amount of any MS-DRG under the IPPS.¹⁷

To qualify for an NTAP, CMS must determine that a product meets all three criteria, including the cost criterion. To satisfy the cost criterion, a new technology or service must result in average charges for cases using the technology in excess of established thresholds for the MS-DRG(s) to which the new technology would be assigned. The threshold equals: the geometric mean charges for the relevant MS-DRG(s) plus the lesser of (1) 75 percent of the standardized amount increased to reflect the difference between costs and charges or (2) 75 percent of 1 standard deviation beyond the geometric mean standardized charge for all cases in the relevant MS-DRG(s). In the proposed rule, CMS summarizes the cost analysis done by each of the four CAR-T NTAP applicants. Each of the four applicants submitted calculations suggesting that their products meet the cost criterion. According to the NRPM, at least one applicant assumed that its new CAR-T product would cost hospitals \$373,000—similar to the prices of existing CAR-T products. The proposed rule sought comment on whether each product meets the cost criterion as well as the criteria for being new and a substantial clinical improvement over existing treatment.

¹⁴ Estimated average sales price (ASP) is imputed based on publicly available payment rate data from the outpatient prospective payment system, which are displayed in Addendum B for January 2021 on the CMS website. The OPSS payment rate of 106 percent of ASP is divided by 1.06 to estimate the ASP for each product.

¹⁵ <https://www.biopharmadive.com/news/gileads-second-act-in-cell-therapy-gets-its-first-approval/582295/>; <https://www.reuters.com/article/us-bluebird-bio-fda/bluebird-bio-sets-list-price-for-multiple-myeloma-therapy-at-419500-idUSKBN2BL1W3>; <https://pharmaphorum.com/news/bms-finally-gets-fda-ok-for-liso-cel-sets-410k-launch-price/#:~:text=Bristol%2DMyers%20Squibb%20finally%20has,of%20large%20B%2Dcell%20lymphoma>.

¹⁶ CMS is also proposing to broaden the definition of MS-DRG 018 to include other immunotherapy products beyond CAR-T products. For example, lifileucel, a tumor-infiltrating lymphocyte therapy for metastatic melanoma patients after progression on multiple therapies, would be included in MS-DRG 018 if approved by FDA. The manufacturer of lifileucel has applied for an NTAP in FY 2022.

¹⁷ The base payment amount for MS-DRG 018 in FY 2021 was roughly \$240,000. Note that the base payment amount will differ from the actual claim payment amount because the labor share of the base rate is wage adjusted, because hospitals may receive additional payments for IME and DSH, and because cases may qualify for outlier payments.

Comment

CAR-T and the NTAP cost criterion

CMS should provide a more detailed discussion of the NTAP cost criterion and whether under the current methodology a new CAR-T product priced similarly to existing CAR-T products can meet the cost criterion. Under current statutory and regulatory NTAP policies, Medicare provides hospitals with extra payments for a limited time period for new, costly technologies that offer a substantial clinical improvement if the MS–DRG payment amount would otherwise be inadequate. Based on the discussion in the proposed rule, it appears that at least one of the new CAR-T products may meet the NTAP cost criterion with a manufacturer price of \$373,000. According to the proposed rule, the manufacturer of a new CAR-T product submitted a cost analysis to CMS that: (1) assumes its product’s cost to the hospital will be \$373,000 and (2) finds, according to the manufacturer’s calculations, that the product would meet the cost criterion. However, with a price of \$373,000, the new product’s price would be similar to the prices of existing CAR-T products that are paid under the existing Chimeric Antigen Receptor (CAR) T-cell Immunotherapy MS–DRG (MS–DRG 018).¹⁸ The possibility that a new CAR-T product with a price similar to existing CAR-T products might meet the cost criterion and qualify for additional payments (over and above what is paid for cases using other, similarly priced CAR-T products) seems inconsistent with the intent of current NTAP policy and the new CAR-T MS–DRG. The discussion of each NTAP applicant’s cost calculations in the proposed rule is not granular enough to discern the different factors that may contribute to this potential outcome, and we urge CMS to provide a more detailed discussion of this issue.

Although the Commission's comment addresses how current NTAP policy is operationalized, we note that the Commission has more general concerns about how Medicare pays for new expensive technology, including drugs and biologicals. As the Commission has previously stated, in general cost criteria provide an incentive for manufacturers and hospitals to increase their prices and charges.¹⁹ In future work, the Commission may examine ways to improve how Medicare pays for new products to better balance manufacturer incentives to innovate with value and affordability for beneficiaries and taxpayers.

CMS should take steps to ensure appropriate use of CAR-Ts and collect evidence on their clinical effectiveness and safety

Although some patients have experienced benefit from CAR-T therapy, given the high cost of currently available products and the potential for significant side effects, CMS should ensure that

¹⁸ According to the proposed rule, the manufacturer of Breyanzi stated that it had not yet determined a price for its product, but the cost analysis submitted by the manufacturer assumed the product’s cost to the hospital will be \$373,000. Although the prices of the other new CAR-T products are not explicitly discussed in the proposed rule, there may be additional CAR-T products applying for an NTAP with prices in this range. For example, press reports for the product Tecartus indicate that its list price is \$373,000 (<https://www.biopharmadive.com/news/gileads-second-act-in-cell-therapy-gets-its-first-approval/582295/>).

¹⁹ Medicare Payment Advisory Commission. 2002. *Report to the Congress: Medicare payment policy*. Washington, DC: MedPAC.

the clinical use of these products is appropriate. To this end, the Commission reiterates our comments from our July 7, 2020, comment letter²⁰ in which we said that the agency should consider implementing a claims monitoring system (as it has done for other services such as outpatient dialysis) to make certain that the use of these therapies is consistent with Medicare's national coverage determination.²¹ The agency should also ensure that the dosing and administration of CAR-Ts is consistent with each product's FDA label. If the Secretary's monitoring system identifies inappropriate use or unusual billing practices, the Secretary should take immediate action. Options that the Secretary could consider include development of local coverage determinations, prepayment and post-payment reviews, provider outreach and education, and program integrity enforcement, as appropriate depending on the nature of any issues identified. Such monitoring efforts would be consistent with efforts taken by some commercial payers to ensure the appropriate use of CAR-Ts, including pre-certification policies.^{22,23}

In addition, the Commission is reiterating its comment from our July 7, 2020, comment letter that CMS reconsider its decision to not implement coverage with evidence development (CED) with a requirement for registry participation for CAR-Ts in its national coverage determination (NCD).²⁴ CED offers the agency an opportunity to generate clinical evidence specifically for Medicare beneficiaries who are older and often underrepresented in trials supporting NTAP applications as well as cancer clinical trials. For example:

²⁰ Medicare Payment Advisory Commission. 2020. Comment letter on CMS's proposed rule entitled "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 2021 Rates; Proposed Quality Reporting Requirements for Specific Providers; Medicare and Medicaid Promoting Interoperability Programs Proposed Requirements for Eligible Hospitals and Critical Access Hospitals; Proposed Rule." July 7.

²¹ According to the NCD for CAR-T, "The Centers for Medicare & Medicaid Services (CMS) covers autologous treatment for cancer with T-cells expressing at least one chimeric antigen receptor (CAR) when administered at healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies (REMS) and used for a medically accepted indication as defined at Social Security Act section 1861(t)(2) i.e., is used for either an FDA-approved indication (according to the FDA-approved label for that product), or for other uses when the product has been FDA-approved and the use is supported in one or more CMS-approved compendia."

<https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=291&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=All&Keyword=car-t&KeywordLookup=Doc&KeywordSearchType=Exact&kq=true&bc=EAAAABAIAAA&>

²² Aetna. 2021. Procedures, program and drugs that require precertification. June.

<https://www.aetna.com/content/dam/aetna/pdfs/health-care-professionals/2021-precert-list-june.pdf>.

²³ Blue Cross Blue Shield Blue Care Network. 2021. Medical Policy Bulletin: Chimeric antigen receptor (CAR)-T cell therapy. April. <https://medpolicy.ibx.com/ibc/Commercial/Pages/Policy/ff1e1eb0-ff93-4459-b3d7-8f94930644ec.aspx>.

²⁴ In its proposed NCD for CAR-T therapies, CMS said that, "We believe the current evidence base, which has significant gaps but demonstrates that CAR T-cell therapy is a promising type of cancer immunotherapy, supports coverage through the CED paradigm for further study in patients with cancer. Accordingly, we believe that patient, product, practitioner, and provider limitations are appropriate at this time in order to maximize the likelihood that Medicare beneficiaries experience a health benefit during and from treatment of their cancer with a CAR T-cell product." (<https://www.cms.gov/medicare-coverage-database/details/nca-proposed-decision-memo.aspx?NCAId=291>.) CMS discussed several factors in its final NCD for CAR-T therapies for eliminating the use of CED and registry participation, including the requirement by the FDA for post-marketing studies and the ongoing research by scientists and manufacturers.

- According to the FDA, “Adults aged 65 years and older, and especially those over age 75, are underrepresented in cancer clinical trials despite representing a growing segment of the population of cancer patients.”²⁵
- In a review of Medicare’s NTAP applications between 2001 and 2016, researchers concluded that patient populations in studies cited by the NTAP applicants were younger, more likely to be male, and more likely to be White than the Medicare population.²⁶

CED could prove useful in generating evidence on the safety of each CAR-T product that is known to have significant risks for neurological toxicities and cytokine release syndrome and reflected in the FDA’s requirements for a REMS program and a black box warning in each product’s labeling. In addition, the FDA is requiring that the manufacturers of all approved CAR-T products (Abecma, Breyanzi, Kymriah, Tecartus, and Yescarta) conduct post-marketing, prospective, multi-center, observational studies to assess the long-term safety and the risk of secondary malignancies occurring after treatment. However, the completion date for these studies is more than 15 years in the future (in 2037 and beyond).²⁷

CED could also be useful in generating clinical evidence about CAR-T products; CMS and researchers have noted the lack of evidence on the effectiveness and safety of CAR-Ts:

- In its national coverage determination for Kymriah and Yescarta, CMS stated that “...the evidence from clinical studies for both tisagenlecleucel and axicabtagene ciloleucel is limited, especially for Medicare beneficiaries 65 years of age and older with a diagnosis of B-cell lymphoma, and weakened by the uncontrolled nature of the studies.”²⁸
- In the FY 2022 proposed rule, CMS raises issues about the clinical evidence included in the NTAP applications submitted by the CAR-T manufacturers; for example:
 - “...we question whether the sample size and research presented in this application [for Tecartus] support extrapolating these results across the Medicare population.”
 - “We question whether, due to the lack of randomization, there is sufficient evidence to establish the efficacy of [Abecma] compared with current alternatives. It is unknown whether the superior outcomes for [Abecma] in the KarMMA study, which has not been peer-reviewed, were due to more effective therapy or other factors, such as differences in patient population or treating oncologist. We also note that the applicant chose to use the [overall response rate] data as a measure of

²⁵ Food and Drug Administration. 2020. Inclusion of older adults in cancer clinical trials: Guidance for industry. <https://www.fda.gov/media/135804/download>.

²⁶ Judson, T., S. Dhruva, and R. Redberg. 2019. Evaluation of technologies approved for supplemental payments in the United States. *British Medical Journal* 365: I2190. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6890455/>.

²⁷ Food and Drug Administration. 2017. Approval letter to Kite Pharma, Incorporated on the manufacturer’s Biologics License Application (BLA) for axicabtagene ciloleucel. October 18.

²⁸ Centers for Medicare & Medicaid Services. 2019. Decision memo for chimeric antigen receptor (CAR) T-cell therapy for cancers. <https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=291&bc=CAAAAAAAAAAAAAAAAA&>

substantial clinical improvement rather than the more clinically relevant and available [overall survival] data.”²⁹

- The 2018 systematic review of Kymriah and Yescarta by the Institute for Clinical and Economic Review (ICER) raised concerns about uncertainty of available evidence. For example:
 - “The studies of CAR-T therapies are all single-arm trials. Given the possibility of selection bias in these trials, it is impossible to compare outcomes from these trials to those of other trials without considerable uncertainty.”
 - “...the trials themselves are small and have short follow-up. The sample sizes with outcomes in the trials are less than 100 participants, and the median follow-up in the trials is less than two years. Thus, estimates of outcomes from the trials have wide confidence intervals; as such, both the benefits and duration of and long-term relapse-free survival is unknown at this point.”
 - “... there may be unanticipated harms that arise as larger numbers of patients are followed for several years.”³⁰
- ICER’s 2021 systematic review of the CAR-Ts that treat multiple myeloma, Abecema and ciltacabtagene autoleucel, concluded that the evidence is insufficient to determine whether one agent is superior to the other. “There are no studies comparing these agents directly, nor sufficient data to perform quantitative indirect comparisons.”³¹

CED enables the program to ultimately develop better, more evidence-based policies.³² Given the limited evidence on the clinical effectiveness of CAR-T therapy among Medicare beneficiaries and the significant neurological toxicities associated with treatment, we urge CMS to reconsider its prior decision not to implement limited evidence on the clinical effectiveness among older Medicare beneficiaries.

²⁹ Centers for Medicare & Medicaid Services, Department of Health and Human Services. 2021. 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 2022 rates; quality programs and Medicare Promoting Interoperability Program requirements for eligible hospitals and critical access hospitals; proposed changes to Medicaid provider enrollment; and proposed changes to the Medicare Shared Savings Program. *Federal Register* 86, no. 88 (May 10): 25070–25130.

³⁰ Institute for Clinical and Economic Review. 2018. Chimeric antigen receptor T-cell therapy for B-cell cancers: Effectiveness and value. Boston, MA: ICER. https://icer.org/wp-content/uploads/2020/10/ICER_CAR_T_Final_Evidence_Report_032318.pdf.

³¹ Institute for Clinical and Economic Review. 2021. Anti B-cell maturation antigen CAR T-cell and antibody drug conjugate therapy for heavily pre-treated relapsed and refractory multiple myeloma. Boston, MA: ICER. https://icer.org/wp-content/uploads/2020/10/ICER_Multiple-Myeloma_Final-Report_051121.pdf.

³² Medicare Payment Advisory Commission. 2018. *Report to the Congress: Medicare and the health care delivery system*. Washington, DC: MedPAC.

Chiquita Brooks-LaSure

Administrator

Page 12

Conclusion

MedPAC appreciates your consideration of these issues. The Commission values the ongoing collaboration between CMS and MedPAC staff on Medicare policy, and we look forward to continuing this relationship. If you have any questions regarding our comments, please do not hesitate to contact James E. Mathews, MedPAC's Executive Director, at 202-220-3700.

Sincerely,

A handwritten signature in black ink, appearing to read "m. chernew", with a horizontal line extending to the right from the end of the signature.

Michael E. Chernew, Ph.D.
Chair