House Committee on Ways and Means Subcommittee on Health
Hearing on Examining Policies that Inhibit Innovation and Patient Access
Written Statement for the Hearing Record

Personalized Medicine Coalition

May 23, 2023

Chairman Buchanan, Ranking Member Doggett, and distinguished members of the Health Subcommittee of the House Committee on Ways and Means, the Personalized Medicine Coalition (PMC) appreciates the opportunity to submit comments on the potential impacts of government policies on medical innovation. PMC is a nonprofit education and advocacy organization comprised of more than 220 institutions from across the health care spectrum who support this growing field. In our following statement, we encourage Congress to thoughtfully consider how policies around drug price negotiations, breakthrough devices, and drugs that receive accelerated approval can incentivize continued innovation in personalized medicine and facilitate patients' timely access to the pharmaceutical, diagnostic, and other technologies underpinning this approach to care.

Personalized medicine, also called precision or individualized medicine, is an evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that impact health. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients. Personalized medicine is playing an important role in transforming care and patient outcomes for a range of serious and life-threatening diseases and conditions, helping to shift patient and provider experiences away from trial-and-error toward a more streamlined process for making clinical decisions. By ensuring that only patients who will benefit from a particular intervention receive it, personalized medicine can also make the health care system more efficient.

As personalized approaches to treatment and prevention have emerged, new types of drugs, tools, and technologies using a patient's genetic and other personal health information have challenged existing regulatory frameworks and processes. Chimeric antigen receptor (CAR) T-cell therapies in oncology, gene therapies for pediatric rare diseases, next-generation sequencing technologies, and biomarker imaging with molecular diagnostics are just a few of the innovations that are unlocking a new era of personalized care. To facilitate patients' timely access to personalized medicine, PMC advocates for flexible coverage policies and adequate payment rates for personalized medicine treatments, diagnostic tools, and technologies that recognize the value these technologies provide to patients, the health care system, and society.

Mitigating Potential Impacts of Medicare's Drug Price Negotiation Program

With the passage of the *Inflation Reduction Act (IRA)* in 2022, Congress gave the Centers for Medicare & Medicaid Services (CMS) the authority to negotiate the prices for certain drugs as soon as 2026. CMS' implementation of the drug price negotiation program represents an

unprecedented new federal authority that will significantly alter how personalized medicine will be evaluated and incentivized under Medicare. Multiple analyses, including those from the Congressional Budget Office, have called attention to the potential consequences of the Medicare drug price negotiation program, such as canceled research and development and disincentives to invest in small molecule medicines and therapeutic areas that require incremental innovation.[i,ii,iii,iv]

Due to smaller patient subpopulations, personalized medicines that address the root causes of disease can sometimes be expensive and risky to develop. Now an important part of health care, personalized medicines have accounted for at least a quarter of new drug approvals for each of the past eight years.[v] In 2022, over half of U.S. Food and Drug Administration (FDA)-approved personalized medicines were indicated for certain cancers, and over one-third were indicated for rare diseases.[vi] There are more than 10,000 rare diseases, including rare cancers, and more than 90 percent of them do not have an FDA-approved treatment.[vii] With companies expected to focus on treatments for larger patient populations where return on investment can be easier, treatment pipelines for cancers and rare diseases are expected to be impacted by Medicare's drug price negotiation program.[viii,ix]

Research conducted after approval of a new drug is important to advancing personalized medicine. After initial approval of a targeted therapy by FDA, further research provides greater understanding of patients' responses to treatment based on results from molecular diagnostics and other biomarkers. This research leads to new or improved treatment indications that contribute to progress in personalized medicine, but smaller patient subpopulations can make it difficult to recoup investment in this research. The potential downstream impacts of the negotiation program are expected to curtail post-approval research.

Over the past eight years, PMC has identified more than 120 expanded indications significant to advancing personalized medicine. Notably, these expanded indications have had an upward trend in the average time since a drug's initial approval. Given this trend, PMC is concerned that implementation of the negotiation program, which by statute makes drug products eligible for negotiation after nine years (or 13 years for biological products), may further stifle post-approval research for expanded indications that provide patients with personalized medicine treatment options. By limiting the exemption of orphan drugs from negotiation to those with only one approved orphan indication for a single disease or condition, the negotiation program could also stifle post-approval research into additional orphan indications for rare disease patients who lack treatments due the risk of losing this exemption.

In March, CMS released its *Medicare Drug Price Negotiation Program Initial Guidance*[x] outlining how the agency will select drugs for negotiation, gather and use relevant data, and carry out the negotiation process to establish a maximum fair price (MFP) for selected drugs for the initial price applicability year (IPAY) of 2026. PMC believes the initial guidance lacks clear descriptions for CMS procedures and methodology. Based on this lack of detail, we are concerned that CMS could implement this new program in ways that unintentionally undermine the incentives for developing innovative medicines, including drugs with personalized medicine treatment strategies that direct them toward patients who are most likely to benefit and away from those who are not. PMC submitted comments to CMS urging the agency to establish a

consistent and transparent methodology for determining a drug's MFP that considers the value of personalized medicine to patients and society and allows a more robust exchange of information with stakeholders that meaningfully considers patients' perspectives on value. While CMS has indicated it plans to release updated guidance as soon as early July, we are concerned that the tight statutory deadlines under the *IRA* for the agency to implement this new program may limit CMS' ability to respond to these and other comments raised by the public.

Medicare's drug price negotiation program could also have an outsized effect on patients' access to new and existing treatments that extends beyond the Medicare program and possibly narrows patients' treatment options. Although Medicare plan sponsors will be required to include selected drugs on their formularies, plans could use restrictive utilization management or other cost-control practices to manage their increased liability and deny coverage for negotiated products vital to a patient's personalized health care. To ensure patients are protected from plan attempts to offset costs, our Coalition has encouraged CMS to establish guardrails and conduct oversight to ensure the clinical appropriateness of any utilization management or formulary changes and to mitigate unintended consequences on beneficiaries' access to both negotiated and non-negotiated drugs.

Congress and the administration should take every step possible to prevent, monitor, and correct for potential impacts of the negotiation program on patients and the health care system. We believe information should be collected on potential unintended impacts to ensure the program does not disincentivize the development of new treatments for unmet medical needs, research on expanded indications that provide additional benefits to patients, or patient access to personalized medicine through cost-control practices.

Facilitating Timelier Medicare Coverage of Breakthrough Devices

A study by the Stanford Byers Center for Biodesign found it takes an average of five years for medical devices to achieve nationwide coding, coverage, and payment.[xi] For devices addressing areas of unmet medical need, the newness of the device and, in some cases, small patient population sizes, can create challenges to gathering the clinical evidence needed for coverage and reimbursement determinations, subsequently increasing the time between introduction to the market and patient access. For personalized medicine to realize its full potential at a moment of rapid progress in science and medicine, patients need timelier access to innovative medical technologies they stand to benefit from.

Devices that receive breakthrough designation and marketing authorization from the FDA provide for more effective treatment or diagnosis of life-threatening or irreversibly debilitating diseases or conditions. A new Medicare coverage pathway expediting patient access to medical products designated as breakthrough devices and authorized by the FDA could mitigate the upfront evidence burden required to meet the current coverage standard while prioritizing patients' unmet medical needs. We believe such a pathway could benefit patients by helping to provide timelier coverage for, and thus access to, certain diagnostic and screening tests as well as other enabling technologies underpinning personalized medicine, such as digital health technologies that leverage artificial intelligence.

Over the past several years, PMC has been engaged on efforts at CMS to develop such a pathway for breakthrough devices. Since the repeal of the Medicare Coverage of Innovative Technology (MCIT) pathway, we have eagerly awaited the Biden Administration's proposed rule on Transitional Coverage for Emerging Technologies (TCET), which was introduced as a replacement for MCIT and was slated to be released in April of 2024. TCET has the potential to provide Medicare beneficiaries access to a broader range of treatment options and to enable patients, in consultation with their doctor, to make informed, personalized decisions about their care. We look forward to reviewing CMS' expected proposal and evaluating its ability to advance personalized medicine.

We believe a successful TCET pathway would be voluntary for breakthrough device manufacturers and would provide predictable coverage at the time of marketing authorization. Timely coverage will improve patients' access to these technologies and facilitate the post-market collection of any additional evidence needed to inform future coverage and reimbursement decisions. To help minimize the burden of post-market evidence collection on device manufacturers, clinicians, and patients, we believe it will be important for this pathway to foster alignment between CMS and the FDA on evidence needs and facilitate early alignment between CMS and device manufacturers on how to resolve any evidence gaps. Providing adequate resources for FDA's and CMS' respective workforces will also be important to help foster this alignment.

CMS has indicated that its forthcoming TCET proposal will build on prior CMS initiatives, such as coverage with evidence development (CED). CMS covers promising therapeutics and services for Medicare beneficiaries under CED on the condition that they are furnished in a setting of ongoing data collection. Although this mechanism has been around for nearly two decades, it lacks transparency in how it is applied, and CMS can require ongoing evidence collection without any specified time frame for retiring these requirements. It is extraordinarily difficult to retire CED requirements.[xii] As a result, CED has created barriers that prevent wider access to medical breakthroughs, limiting data for research and ultimately hampering innovation.[xiii] Thus, PMC is concerned that if CMS requires CED for breakthrough devices because limited initial evidence is available, CED could diminish the potential for the TCET pathway to improve patients' access to personalized medicine. To resolve some of the challenges and uncertainties with CED, CMS must include a time limit for any evidence collection requirements.

PMC believes breakthrough devices should also be eligible for coverage under the TCET pathway regardless of whether they fall within a defined benefit category. Some diagnostic and screening tests, like those used for preventive screening, may not fall within a defined Medicare benefit category. In developing a new coverage pathway within its existing authorities, we recognize that CMS faces statutory constraints in providing coverage for breakthrough devices that do not fall within a defined Medicare benefit category. For this reason, we have previously supported the inclusion of a provision in legislation introduced in the previous Congress that would codify a transitional coverage and payment pathway for breakthrough devices under the Medicare program, including for "specified" breakthrough devices that do not fall into a defined Medicare benefit category.

Ensuring the Accelerated Approval Pathway Continues to Benefit Patients

To realize the benefits of rapid advances in science and facilitate patients' access to new treatments in a timely manner, the regulatory approval processes in the United States have evolved. As one of four expedited pathways available at FDA, the Accelerated Approval Program allows FDA to approve certain drugs that treat serious or life-threatening diseases and offer meaningful therapeutic benefit to patients over existing treatments before confirmatory trials are completed. Between 2011 and 2017, the majority of newly approved drugs were associated with at least one expedited FDA review pathway.[xiv] With the increasing identification of new molecular drug targets, the use of these pathways in personalized medicine is expected to grow. As of March 2023, FDA had approved 295 products under accelerated approval, including numerous drugs for patients with cancers and rare conditions like sickle cell disease or Duchenne muscular dystrophy.[xv] Dozens of these treatments have been personalized medicines.

Accelerated approval is critical for providing patients with access to new safe and effective drugs that fill unmet medical needs. Since its inception in 1992, millions of patients with serious or life-threatening illnesses have received faster access to new drugs and better outcomes under the program.[xvi] For patients with progressive diseases and unmet medical needs, time is of the essence. In cancer, accelerated approval can give patients access to new treatments around four years faster on average and as much as 12 years faster for certain drugs.[xvii] With more than 90 percent of rare diseases lacking an FDA-approved treatment, timelier access to novel treatments can offer meaningful advantages in treating or managing a patient's disease.

To gain approval in this pathway, a drug must still meet FDA's standards for safety and efficacy. Accelerated approval simply permits FDA to accept a different type of data when deciding that a drug's benefits outweighs its risks. While traditional approval relies on a direct demonstration of clinical benefit, accelerated approval relies on surrogate or intermediate clinical endpoints that are expected to predict clinical benefit and can be measured earlier in shorter, smaller clinical trials. Under accelerated approval, FDA accepts a level of uncertainty that the surrogate endpoint will not be confirmed to be predictive of clinical benefit. In order to resolve those uncertainties, FDA requires drug companies to conduct confirmatory studies after approval. Validated surrogate endpoints and post-marketing requirements can also be associated with drugs that received traditional approval, so these features are not unique to the accelerated approval pathway.

Designing, enrolling, and completing post-marketing studies can be very complex. Limited understandings of a disease, small numbers of patients, and a lack of regulatory precedent can also create challenges in evaluating the long-term clinical benefit of new drugs. Although the accelerated approval pathway has been criticized due to delays in the completion of confirmatory studies and a failure to complete some studies by sponsors, the pathway has been largely successful in bringing to market treatments where the expected clinical benefit of the drug was confirmed. One analysis has estimated that 33 percent to 66 percent of products approved under the Accelerated Approval Program may not have come to market or been developed at all without the flexibilities available through this pathway.[xviii]

Earlier this year, in response to President Biden's executive order on lowering prescription drug costs, the CMS Innovation Center (CMMI) announced it would consider for testing a new Accelerating Clinical Evidence Model. This mandatory model would aim to incentivize manufacturers to complete confirmatory trials for their drugs approved under the Accelerated Approval Program by adjusting payments to providers. In 2022, Congress also granted new authorities to FDA to ensure that sponsors of accelerated approval drugs are complying with post-approval requirements, and the effect of these authorities in resolving concerns with the completion of confirmatory studies has yet to be realized. Coupled with the new drug price negotiation program, the Accelerating Clinical Evidence Model could further force manufacturers to limit research into expanding drugs' indications for unmet medical needs and shift investment away from disease areas where treatments are more difficult to develop under traditional approval.

Accelerated approval offers a vital approach for advancing treatments for patients with diseases that stand to benefit from advances in personalized medicine. We encourage Congress to protect this pathway to ensure that personalized medicines can be reviewed in a flexible and timely manner by FDA and provide greater opportunities for novel drug development to benefit patients.

Conclusion

PMC appreciates the opportunity to discuss the potential impacts of government policies on innovation and patient access to personalized medicine. We look forward to working with Congress on policies that improve the health care system and bring us closer to a future in which every patient has access to and benefits from an individualized approach to health care.

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