PERSONALIZED MEDICINE COALITION

July 16, 2018

The Honorable Alex Azar
Secretary
Department of Health and Human Services
200 Independence Avenue, SW, Room 600E
Washington, D.C. 20201

Sent electronically

RE: Request for Information (RFI) on the Department of Health and Human Services (HHS) Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs (RIN 0991-ZA49)

Dear Secretary Azar:

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 Department of Health and Human Services (HHS) Request for Information (RFI) on its Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs.[i] PMC recognizes the intent of the proposal is to lessen the financial burden of drug costs on American patients and their families. To achieve this goal and sustain progress toward personalized treatment strategies that benefit patients, we urge HHS to address issues we have found with the Blueprint, which are identified below, and continue activities to improve access to innovative medical products by focusing on value-based arrangements based on patient-centered assessments of value.

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. 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.

Statement of Neutrality

Many of PMC's members will present their own responses to HHS 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 RFI.

Comments on the Current Structure and Function of the Pharmaceutical Market

The introduction to Section III of the RFI states that "HHS is interested in public comments about the general structure and function of the pharmaceutical market" to inform the department's actions. PMC recently released *Personalized Medicine at FDA: 2017 Progress Report,* [ii] which demonstrates how personalized medicine has reshaped drug development over the last decade in ways that are benefiting patients. Our report documents a record number of new personalized medicine approvals by FDA, including the first three gene therapies ever approved in the U.S. and the first personalized medicine biosimilar. This marks the fourth consecutive year that personalized medicines accounted for more than 20 percent of all new drug approvals. Fortunately for patients, the pipeline for significant personalized therapies is also 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.[iii]

Many of the personalized medicines approved by the FDA and those in the pipeline are for patients with diseases and conditions that have very poor prognoses like advanced breast cancer, non-small cell lung cancer, leukemia, lymphoma, and cystic fibrosis, among others. Advances in science made possible through significant investment from government and the biopharmaceutical industry have transformed once-deadly diseases into manageable chronic conditions for some patients.

As the department contemplates activities to reduce drug costs and out-of-pocket expenses, we ask that you remain cognizant of the fact that a one-size-fits-all, trial-and-error approach to treatment can rob patients of time and reduce their quality of life.[iv] This approach to treatment also stands in contrast to the direction of medical product development, which is focusing more on therapeutics that define patient populations based on biological signatures and other factors that may influence an individual patient's response.

Comments on the Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs

Request for Formal Rule-Making Process

Each of the proposals mentioned in the RFI will impact patient access to FDA-approved treatments and, if implemented, lay the foundation for a reimbursement environment that may affect access to other novel treatments. We are concerned that proposals are described "for administrative action, when within agency authority," in the introduction to Section III of the RFI. Because the Blueprint proposals lack the detail needed to truly vet them via the regulatory process, we request that the formal rule-making process be used as the department explores each option to lower drug prices and reduce out-of-pocket costs, including any demonstrations proposed through the Center for Medicare & Medicaid Innovation (CMMI). The rule-making process would allow ample time for stakeholder consideration and comments.

Shifting Medicare Part B Drugs to Part D

Section III. B. of the RFI emphasizes a desire to further explore proposals introduced in the President's FY 2019 Budget to shift some Medicare Part B drugs to Medicare Part D. Many of the drugs currently in Part B are personalized medicines. We understand that the department believes that moving the reimbursement of physician-administered drugs from Part B to Part D has the best promise of constraining the costs of high-priced medicines, but we are concerned that this proposal may result in increased costs to patients, access barriers for patients and providers, and unintended safety issues.

Under Part B, patients pay a deductible and cost sharing – which is often covered by a supplemental health plan (Medigap) or Medicare Advantage. But the standard Part D benefit in 2017 included a deductible, followed by 25 percent coinsurance for prescriptions up to an initial coverage limit, and then a coverage gap where patients without low-income subsidies (LIS) paid a larger share of their drug costs until their out-of-pocket drug spending exceeded a catastrophic coverage threshold. Once a patients' drug spending reached the catastrophic threshold, those without the LIS paid up to 5 percent of their total drug costs. [v] Under Part D with no out-of-pocket limit on cost sharing, patients could face bills for a drug they are taking for a prolonged period of time. A comprehensive study to model Part B to D consolidation found that, even when drug categories were carefully selected, Medicare beneficiaries invariably paid more for their treatments under Part D. While the model did show overall savings to the Medicare program, for two of the six categories, increased patient costs were not offset with likely Medicare savings.[vi] Depending on the scope of the proposed change, movement of higher-priced Part B drugs to Part D could also increase costs for all beneficiaries and subject many beneficiaries to higher out-of-pocket costs due to the benefit design of Part D.

In addition to increasing costs for patients, moving Part B drugs to Part D could impact how the drugs are administered and possibly compromise patient safety. Most Part B drugs are physician-administered, while beneficiaries in Part D generally pick up drugs at pharmacy or receive them through mail-order services. This will not work for some Part B drugs, because they are for infusion and can be temperature sensitive. These drugs require particular handling, and altering could undermine the efficacy of the treatment. Blood work may also be required before infusion of some Part B drugs, and patients often need to be monitored after treatment. In this proposal, it is unclear how Medicare would ensure proper handling of Part B drugs if they were switched to Part D and alleviate the increased financial burden to patients that may be associated with the switch.

We recognize that the high cost of drugs in Part B is a problem for which there is no single fix. We expect that CMS' implementation of the Quality Payment Program, particularly its inclusion of a "cost" category within the Merit-Based Incentive Payment Program (MIPS) and movement toward shared risk in Alternative Payment Models (APMs), will reduce or eliminate existing clinician incentives toward selection of higher-cost treatment options and accomplish the goal of improving care while reducing costs. While PMC understands that the department is looking for additional solutions, we believe moving Part B drugs into Part D without sufficient safeguards will have a negative impact on patients.

Fostering Value-Based Arrangements

Section III. B. of the RFI highlights ways in which the department would like to experiment with value-based purchasing in federal programs. We generally support HHS' interest in testing new models of care

if they enhance the alignment of incentives; incorporate key perspectives to define high-value care; focus on outcomes that matter to patients; and construct efficient arrangements between payers, drug manufacturers, and other stakeholders.

In 2017, PMC published *Personalized Medicine and Value Assessment Frameworks: Context, Considerations, and Next Steps*.[vii] The white paper contends that to improve clinical outcomes and facilitate more cost-effective health care, frameworks used to assess value must incorporate the principles of personalized medicine. We examined the characteristics of U.S.-centered value assessment frameworks (VAFs) and identified how each integrates — or fails to integrate — personalized medicine.

Both public and private payers have expressed an interest in the use of VAFs for coverage and payment decision-making. This has increased the likelihood that VAFs will impact access to care. PMC believes that to facilitate access to treatment options of the highest value at both the individual patient and health care system levels, VAFs must consider the perspectives of payers, providers, and patients. Unfortunately, the frameworks in use today do not incorporate all of these perspectives.

As the department explores value-based payment strategies, the question of how value is assessed must be answered. We hope that specific limitations in current VAFs are addressed to ensure alignment of value-based arrangements with the value elements of personalized medicine, in preparation for the increasingly predominant role it will have in health care. PMC urges the department to follow the recommendations from our white paper as it experiments further with modifying existing and developing new value-based arrangements as part of the Blueprint. Our recommendations are that:

- Diagnostic testing is considered as an explicit and integral part of the value assessment of treatment options where efficacy and/or safety information can be obtained;

- Formal mechanisms for consideration of heterogeneity of treatment response are integrated and appropriately balanced with population-based considerations;

- Methods for the consideration of emerging or evolving elements of value over time are developed to fully account for emergent benefits at the health system and individual patient levels;

- Appropriate awareness and education takes place about the use of value assessment frameworks in personalized medicine to reduce the risk of inappropriate restriction of reimbursement and/or access to individualized care; and

- Perspectives of all stakeholders are considered, especially patients.

Driving Efficiency, Lowering Costs and Improving Care with Diagnostics

A recent survey of physicians published in the *American Journal on Managed Care Physicians* identified eight conditions that have had the greatest effect on morbidity and mortality since 1990. The conditions identified include breast cancer, ischemic heart disease, HIV, diabetes, unipolar depression, chronic obstructive pulmonary disease, cerebrovascular disease, and lung cancer. In assessing interventions that have made the most significant impact across these conditions, the physicians surveyed considered pharmaceuticals and biopharmaceuticals as having the greatest post-diagnosis effect. Diagnostics

delivered the second largest effect at 20 percent. [viii] Results like these highlight the increasingly important role diagnostics play in improving patient health and how integral they are to the practice of health care.

Personalized medicine presents an opportunity for the whole health care system to operate more efficiently. It has the potential to control health care costs by identifying the right drug for a patient — including, where appropriate, lower-cost generic drugs. Personalized medicine can also reduce health care costs if molecular diagnostic tests are performed on non-invasive samples, such as peripheral blood, or if a few cells are taken by fine needle aspiration, as these types of tests can eliminate the need for costlier surgeries.

In many disease areas, diagnostic tests enable physicians to identify the most effective treatment for a patient immediately by testing for specific molecular characteristics. Medicines that target those molecular characteristics often improve patient outcomes and reduce side effects. One of the most common applications of this practice has been for women with breast cancer. About 30 percent of breast cancer cases are characterized by over-expression of a cell-surface protein called human epidermal growth factor receptor 2 (HER2). For breast cancer patients who express this molecule, adding an antibody drug like trastuzumab to their chemotherapy regimen can reduce their recurrence risk by 52 percent.[ix] [x] Molecular diagnostic tests for HER2 are used to identify the patients who will benefit from receiving trastuzumab and other drugs that target HER2, such as lapatinib. Treatments targeting genetic variants involved in the molecular pathway of disease, such as BRAF in melanoma and ALK and EGFR in non-small cell lung cancer, represent a remarkable improvement, and the field is moving toward an era in which all cancer cases are met with a targeted course of treatment.[xi]

Other personalized medicine tests measure prognostic markers that help indicate how a disease may develop in a person when a disorder is already diagnosed. For example, two complex tests use prognostic markers to help physicians target the best course of treatment for breast cancer patients. One test can determine whether women with certain types of breast cancer are likely to benefit from chemotherapy.[xii] [xiii] [xiv] The other test can detect which early-stage breast cancer patients are at risk of distant recurrence following surgery.[xv] [xvi] Both tests place patients into risk categories that inform physicians and patients of whether the cancer may be treated successfully with hormone therapy alone, as opposed to some combination of hormone therapy and chemotherapy, which is associated with an additional financial burden and toxic effects.

As highlighted in PMC's report *The Future of Coverage and Payment for Personalized Medicine Diagnostics,* personalized medicine can ultimately control costs and improve outcomes when we know the right combination of drugs to provide long-term disease control. A well-established example is the case of protease inhibitor and other anti-retroviral drug cocktails for HIV. For patients using these drugs, molecular diagnostics play a fundamental role in effective management. Initially, drugs can be selected based on molecular predictive profiling of the HIV virus affecting a particular patient; subsequently and on a monthly basis, the effectiveness of the drugs can be rapidly ascertained by measuring HIV viral load in peripheral blood. [xvii]

Personalized medicine is even allowing the ability to uncover molecular markers that signal disease risk or presence before clinical signs and symptoms appear, offering an opportunity to focus on prevention and early intervention rather than on reaction at advanced stages of disease. In some areas, early genetic testing can save lives. For example, women with certain BRCA1 or BRCA2 gene variations have up to an

85 percent lifetime chance of developing breast cancer, compared to a 13 percent chance among the general female population.[xviii] [xix] [xx] Women with harmful BRCA1 and BRCA2 mutations also have up to a 39 and 17 percent chance, respectively, of developing ovarian cancer, compared with a 1.3 percent chance among the general female population.[xxi] The BRCA1 and BRCA2 genetic tests can guide preventive measures, such as prophylactic surgery, chemoprevention, and more frequent mammography. Personalized medicine also opens the door to early intervention for patients with familial hypercholesterolemia, which is characterized by a mutation in the LDL receptor gene. These patients can take PCSK9 inhibitor drugs that block the PCSK9 gene to reduce their cholesterol levels and potentially decrease their risk of developing coronary artery disease.

Although the use of diagnostic tests has been steadily rising in drug development and for the diagnosis, treatment and prevention of diseases, coding, coverage, and reimbursement barriers still exist for these technologies. Diagnostic tests are not specifically referenced in the Blueprint. PMC encourages the department to thoughtfully address barriers facing the diagnostic space under Section III. E. of the RFI.

CMMI New Directions

CMMI is not specifically referenced in the RFI. Given the impact that proposed changes to federal and state programs related to prescription drugs in the Blueprint could have on patient care as well as CMMI's mandate to test innovative payment and service delivery models to reduce program expenditures while preserving or enhancing the quality of care, we expect that CMMI will play a significant role in Blueprint implementation.

PMC responded to CMS' RFI on "New Directions" for the Innovation Center in November of 2017.[xxii] In our comments, we expressed concern that poorly developed or vetted large-scale payment and service models could negatively impact care delivery. We commended CMS for re-examining the direction of the Innovation Center and shared that the guiding principles laid out in the "New Directions" RFI provided reasonable assurance that the Innovation Center plans to proceed at a more measured pace with an eye toward increased transparency and broader participation in value-based model design. PMC proposed several recommendations to ensure that future payment and delivery models tested by the Innovation Center foster the adoption of personalized medicine. We also suggested program improvements for the Innovation Center that would enhance transparency to foster broader stakeholder engagement.

CMS has publicly posted comments received during the open comment period on the Innovation Center website. In April, the agency also announced that it is considering a direct provider contracting model as a result of the feedback received during the "New Directions" RFI comment period. CMS has not announced, however, how it will respond to other recommendations for improvements highlighted in RFI responses received from more than 1,000 stakeholders.

PMC believes that personalized medicine can help CMS deliver affordable, accessible health care that puts patients first. But that will happen only if models of care are not rooted in current standards of care, instead allowing providers the flexibility to maximize individual patient outcomes by tailoring care to a patient's genetics and other factors. If the department is considering CMMI as a mechanism for testing payment and care delivery models connected to Blueprint implementation, under Section III. E. of the RFI we ask that you require CMMI to provide an update on how it plans to incorporate insights received from the public on

improvements to existing models and ways of testing new models that empower patients with more choices and help them achieve better health outcomes.

Conclusion

Thank you for your leadership and for considering our comments. As HHS moves forward with implementation of its Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs, we urge you to ensure that the actions taken bring us closer to the goal PMC shares with the department of delivering innovative, 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

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