



**VIA ELECTRONIC DELIVERY**

July 20, 2020

Ms. Seema Verma  
Administrator  
Centers for Medicare and Medicaid Services  
Department of Health and Human Services  
Attn: **CMS-2482-P**  
Mail Stop C4-26-05  
7500 Security Blvd  
Baltimore, MD 21244

**Re: Proposed Rule, Medicaid Program; Establishing Minimum Standards in Medicaid State Drug Utilization Review (DUR) and Supporting Value-Based Purchasing (VBP) for Covered Drugs in Medicaid, Revising Medicaid Drug and Third-Party Liability (TPL) Requirements [CMS-2482-P]**

Dear Administrator Verma:

I am writing on behalf of the Biotechnology Innovation Organization (BIO) relating to the issuance of a proposed rule by the Centers for Medicare and Medicaid Services (CMS) that would make several changes in the reimbursement and payment structures of the Medicaid program "(Proposed Rule)."<sup>1</sup> We would particularly like to provide comment on CMS' proposed changes to the calculation of Best Price in relation to the use of certain Value-Based Purchasing arrangements (VBP), the regulations governing the exclusion of manufacturer-sponsored copayment assistance programs from Average Manufacturer Price (AMP) and Best Price, and the definition of line extension, new formulation, and oral solid dosage form for purposes of calculating the alternative rebate for line extensions under the Medicaid program.

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than thirty other nations. BIO's members develop medical products and technologies to treat patients afflicted with serious diseases, to delay the onset of these diseases, or to prevent them in the first place. In that way, our members' novel therapeutics, vaccines, and diagnostics yield not only improved health outcomes, but also reduced health care expenditures due to fewer physician office visits, hospitalizations, and surgical interventions.

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<sup>1</sup> 85 Fed. Reg. 37286 (June 19, 2020).

Many of BIO's members are developing complex and transformative therapies that stand to revolutionize the treatment and prevention of both rare and non-rare diseases. These products -- complex, potentially curative, and with a potential impact on short-term payer budgets due to many products having a one-time administration and long-term value -- are ill-suited for the traditional fee-for-service reimbursement environment established more than 50 years ago for government healthcare programs. As such, BIO has been leading the charge in pushing for advances in policies to pay for value rather than volume. CMS is no doubt aware of the many meetings and letters BIO has provided to various offices at the Agency regarding a need to focus on value-based payment, and we appreciate CMS' efforts to move in the direction of evolving payment and recognizing the value many of these new and complex therapies can have. We applaud the Agency on this front, and we look forward to working with CMS as the VBP provision of this rule moves forward and evolves to address BIO's operational concerns and the Agency acknowledges may exist.

Notwithstanding our support for the provisions that would assist the advancement of VBPs, we are strongly opposed to the Agency's proposals for line extensions and copay accumulators, as these proposals will have negative impacts on patient access to innovative medicines. At a minimum, we believe that these provisions should be severed from the VBP provisions of the rule and considered through separate rulemaking.

Our overall comments in this letter can be summarized as follows:

- **These proposed changes related to VBPs are an important first step in the adoption of voluntary VBPs, which BIO supports, but additional clarity from both CMS and OIG is necessary to ensure broader use. Continued work between CMS, the states, and biopharmaceutical manufacturers is necessary to ensure proper operationalization of the new price reporting requirements and so states and manufacturers can build the appropriate infrastructure.**
- **Given the impact on Best Price, additional guidance will be necessary, through coordination with HRSA, in order to address the impact on the 340B Drug Pricing Program.**
- **The VBP provisions should be decoupled from other provisions of the proposed rule in any future rulemaking and finalized as soon as CMS can make BIO's suggested clarifications, and the additional operational challenges can be resolved through future rulemaking and guidance. This will provide Medicaid Agencies with the necessary flexibility to implement payment models for innovative transformative therapies that are coming to market in the short term.**
- **CMS' proposal to modify the Best Price exclusion criteria to account for PBM accumulator programs misreads the statutory definition Best Price, is operationally infeasible, would increase**

**the out-of-pocket costs for patients in PBM accumulator programs, and would threaten patient's access to their medicines; and,**

- **New definitions of "line extension" and "new formulation" are not consistent with statutory language and will severely stymie new drug innovation and harm patient access to potentially life-saving treatments.**

### ***Value-Based Purchasing Arrangements***

For years, BIO and our members have expressed great interest in value-based arrangements (VBP) under which payment for a prescription drug or biologic could vary depending on its outcome for any particular patient. We view these arrangements as critical to fostering a biotechnology environment that encourages innovation in research and development, while simultaneously balancing the need for payers to have avenues to spread risk and to associate payments with the value provided to any individual patient. Our industry has sought to partner with payers and health care providers to structure a variety of innovative payment arrangements that have proven valuable for patient access and for supporting ongoing innovation that will improve patient outcomes, and in many cases, cost.<sup>2</sup> Further, several state Medicaid programs—including Alabama, Arizona, Washington, Oklahoma, Michigan, Colorado, Louisiana, and Massachusetts— have received CMS approval to enter into VBP contracts with drug manufacturers in recent years. However, across all payer segments, uptake has been limited due, in part, to the barriers posed by government price reporting requirements like Medicaid Best Price and Average Manufacturer Price (AMP). To that end, we support CMS' proposal to address existing barriers in the Medicaid Drug Rebate Statute thereby encouraging the advancement of VBPs. Below we outline a number of recommendations to improve upon CMS' approach.

CMS has proposed two different methods to report Best Price in the context of a VBP: (1) a bundled sale, which manufacturers have already successfully utilized for VBP development, and (2) use of multiple Best Prices to account for varied health outcomes over-time of individual patients. While the bundled sale approach validates manufacturers' previous reasonable assumptions, the multiple Best Price scenario is new, and therefore requires consideration and additional information for successful implementation.

In addition, given the challenges to establishing metrics and that states may vary in their ability to collect data and implement such contracts, as discussed below, manufacturers must be assured that the offering of a VBP to a state Medicaid agency is voluntary and not required by the proposed regulation. BIO

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<sup>2</sup> See e.g.

<https://www.mckinsey.com/~/media/McKinsey/Industries/Pharmaceuticals%20and%20Medical%20Products/Our%20Insights/Innovative%20pharma%20contracts%20When%20do%20value%20based%20arrangements%20work/Innovative-pharma-contracts-When-do-value-based-arrangements-work.pdf>

also urges CMS to confirm that the choice to utilize the multiple Best Price approach or the bundled sale approach is voluntary on the part of the manufacturer. As such, CMS should clarify that the lack of a VBP does not release the state from the coverage obligations of § 1927 of the Social Security Act.

### *Bundled Sale*

BIO is pleased to see that CMS has proposed to codify in regulation a principle that the biopharmaceutical industry has always understood to be the case – that contingent value-based concessions may be addressed in price reporting through the bundled sales methodology. Thus, BIO strongly supports the addition of VBP explicitly into the definition of a “bundled sale.” Though some manufacturers have implemented such models through reasonable assumptions, codifying the ability to do so in a Final Rule will improve consistency and predictability, and diminish legal risk, for manufacturers moving forward. In doing so, CMS should confirm longstanding practices of manufacturers with respect to reasonable assumptions and bundled sales for VBPs. We urge CMS to clarify and confirm that if a manufacturer were to determine that it appropriately could account for a VBP through adherence to CMS’s bundled sales rules, the manufacturer would not need to calculate and report multiple Best Prices. Furthermore, BIO believes the “bundled sale” definition ought not limit an outcomes-based measurement metric to creating a bundle, as opposed to using the multiple Best Price approach, if the VBP meets the definition of a “value-based purchasing arrangement,” which includes the requirement that the price concession is “substantially” linked to the outcomes-based measure.

It is important to emphasize, however, that covered outpatient drugs indicated for rare diseases and sold under a VBP will not have enough volume with individual payers to use this bundled sale pathway. For example, many gene therapy on or approaching the market will be indicated for disorders or specific phenotypes of such populations that have extremely low prevalence, such as spinal muscular atrophy, sickle cell disease, muscular dystrophies, adults with severe hemophilia A and B, and the multitude of lysosomal storage disorders. Indeed, covered outpatient drugs for such indications sold under a VBP would *only* be able to avail themselves of the proposed multiple best price pathway to prevent refunds or reimbursements triggered by non-responding patients from potentially skewing their quarterly reported best price.

### *Restatements Beyond 12-Quarters*

BIO supports the provision that would allow manufacturers engaged in a VBP that extends beyond the three-year window to restate their Best Price and the Average Manufacturer’s Price more than 12-quarters from the initial sale. A key obstacle to the adoption of pay-over-time VBPs is the fact that these VBPs would depend upon patient outcomes being monitored and reported over the long-term. Yet, the long-term outcomes metrics with respect to certain therapies are often not readily apparent within a three-year timeframe. Given the potential long-term

durability of gene therapies, payers and manufacturers may want to enter into VBPs with a measurement period of greater than three years; the restatement period should not be an arbitrary barrier to that. We urge CMS to confirm that entering into VBP arrangements with a duration longer than 3 years, and thus potentially implicating restatements beyond 12-quarters, is voluntary and at the manufacturer's discretion.

### *Multiple Best Price Development and Operationalization Challenges*

As we discussed above, the second proposed methodology to allow for multiple Best Prices for a single NDC-9 is novel. CMS proposes that "a single drug may be available at multiple price points, each of which may establish a 'Best Price' based on the relevant or applicable VBP arrangement and patient evidence-based or outcome based measures"<sup>3</sup> We agree with this approach and believe it will help facilitate the use of VBP arrangements across the marketplace. We share CMS' sentiment that this proposal could pose difficulties in implementation. To ensure the final provision provides manufacturers and payers the needed flexibility to implement novel VBP arrangements, we ask CMS to issue additional guidance surrounding some key questions. Some of the questions include, but are not limited to:

- Manufacturers Processes and Government Pricing Systems are all designed to calculate and store a single Best Price and Unit Rebate Amount for each drug for a reporting period; this change will require changes to processes and IT system upgrades. Manufacturers will need additional guidance as to how the varying Best Price reporting will work and may need time to implement prior to the change becoming effective.
- CMS Medicaid and State Medicaid Processes need to be updated to support the change, and as above, manufacturers will need to understand the timing and an implementation plan for such changes.
- 340B Drug Discount Program – key questions need to be addressed regarding how ceiling prices should be calculated under VBP arrangements.

CMS will need to consider state Medicaid program infrastructure in determining how to successfully implement the proposal. Specifically, it seems unclear how patients on the drug would be assigned to the VBP contract or the standard rebate agreement. In addition, some of the complex challenges that manufacturers and payers, including states, may need to overcome when negotiating these agreements include, but are not limited to:

- Selecting the right outcome: Research indicates that an outcome needs to be meaningful (to payers, providers, patients and

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<sup>3</sup> 85 Fed. Reg. at 37293.

- manufacturers); measurable within a reasonable timeframe; readily available (i.e. claims data); and, not be subject to variability.<sup>4</sup>
- Flexibility: Not all therapeutics or disease areas will be ideal for a VBP because a "good/right" outcome may not be available that is appropriate for a real-world setting. This is particularly true in certain rare diseases that progress slowly with heterogenous populations. One particular outcome may not be reflective of the entire population. This further illustrates the importance of VBPs being voluntary with maximum flexibility provided for manufacturer and payer, including State Medicaid programs, to develop agreed-upon terms.
  - Patient tracking: There is a need to ensure that payers, including State Medicaid programs, have a responsibility to track patients as part of a VBP contract. Issues include patient portability or patients lost to follow-up, which likely means treatment success. Payers have to be equal partners and the responsibility of tracking patients will be a mutual one between manufacturers and payers.

The difficulty and the risk involved in developing these metrics for a manufacturer and the state or other payer demonstrates why VBPs must be voluntary for both the state and the manufacturer, as noted above.

Similarly, given the rebate statute's requirement that all beneficiaries receive the same benefit as measured in "amount, duration and scope," we would encourage CMS to clarify this standard when assessed within VBP versus non-VBP programs.<sup>5</sup> We also would urge CMS to work with states to develop the necessary infrastructure and data collection programs that can accurately monitor health outcomes and assess cost savings as noted above. This data will be critical in successfully facilitating the rebate exchanges calculated with some evidence-based or outcomes-based metrics. Furthermore, the operational challenges might require that manufacturers directly contract with states, which is not currently envisioned by the standard National Rebate Agreement, in order to ensure they receive the data necessary to administer a VBP. A direct agreement with the state may also provide important legal protections, provide clarity, and reduce disputes.

### *Average Sales Price (ASP)*

BIO also seeks additional clarity on the Best Price interplay with other government pricing policies, including Medicare Part B ASP. Specifically, while ASP excludes sales that are otherwise excluded from Best Price<sup>6</sup>, since VBP discounts will necessarily be *included* in the multiple Best Price proposal for

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<sup>4</sup> Massachusetts Institute of Technology has done good work in this area. See MIT work here: <http://newdigs.mit.edu/sites/default/files/FoCUS%20Research%20Brief%202018F211v028.pdf>

<sup>5</sup> See generally 42 U.S.C. § 1396a.

<sup>6</sup> SSA § 1847A(c)(2).

states that participate in the VBP (but excluded for states that do not participate in the VBP), it is not clear how this will impact calculation of ASP – particularly since ASP/Part B program rules will not currently involve their own VBP. We urge CMS to confirm that manufacturers may continue to rely on ASP reasonable assumptions, while manufacturers work with CMS to provide further input on what to do about ASP calculations.

### *340B Drug Pricing Program*

Similar to the interplay with ASP is the impact of Best Price on the ceiling price applicable to covered entities under the 340B drug discount program. Given the statutory calculation for ceiling price marrying components of the Medicaid rebate statute, the Best Price calculation of any individual product is critical.<sup>7</sup> In assessing the statutory mandate of the 340B program –to assure access to medicines to certain vulnerable populations – it is not clear that a stand-alone VBP program is applicable to or even necessary for 340B utilization. Before any approach requiring multiple Best Prices is finalized, we would urge CMS and the Health Resources and Services Administration (HRSA) to clarify, through additional rulemaking how the 340B ceiling price should be calculated under such a price reporting mechanism. We believe any additional guidance should be done concurrently with any potentially finalized VBP rule.

Another aspect of the 340B program relates to timing of the Best Price reporting and revisions. This is likely to change given the proposed updates to Best Price to account for the VBP models that will be developed. Manufacturers and covered entities alike will need updated guidance on how to handle Best Price revisions in the context of updates to 340B ceiling pricing in order to permit robust adoption of these programs while also allowing for compliance with other programmatic requirements. Given these considerations, in addition to the likely impact other provisions of this NPRM, such as line extensions will have on the 340B Program, BIO urges CMS to work with HRSA to ensure manufacturers and covered entities have proper rulemaking or guidance to ensure the integrity of the 340B Drug Pricing Program. We would urge this rulemaking or guidance to be issued concurrently to a Final Rule codifying the proposed VBP provisions.

### *Definition of VBPs*

In this Proposed Rule's preamble, CMS has asked for comment on the definition of VBPs. BIO believes that the definition should be broadened to allow for the flexibility to encompass VBP and alternative payment arrangements that may not currently be anticipated by the Proposed Rule, such as the measurement of patient adherence to a drug regimen, capping of drug costs based on defined events, shared savings or shared loss arrangements, and so-called subscription model arrangements. Moreover, CMS should ensure any VBP definition allows for population-based arrangements or patient-specific arrangements. In addition,

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<sup>7</sup> See 42 U.S.C. § 256b(a)(2)(A).

CMS should clarify that any associated data analytics arrangements necessary to measure the VBP are not themselves considered a price concession, as data analytics are often a necessary component to a VBP to measure whether an outcome or other defined endpoint to the VBP has been met. Moreover, CMS asks for comment on the term “substantially linked” and whether payment should be 90% linked to the outcomes of the drug. We do not believe it is appropriate to place a percentage link because there are many types of VBPs and placing an arbitrary percentage would unnecessarily exclude multiple types of agreements that could be agreed upon and entered into, thereby stymying innovation in VBPs. We also urge CMS to strike “substantially” because it is unnecessary to further define the link to evidence or outcomes, and would unnecessarily impinge upon the flexibility of the parties in negotiating VBPs.

There are other aspects of alternative payment models we would urge CMS to consider as part of the definition to allow for the flexibility to include other types of arrangements that are not necessarily tied to clinical metrics. For instance, some payment models in the commercial space are not limited to outcomes-tied performance contracts. Some other programs, for instance, structure payments as a “pay-over-time,” but not tied to any individual clinical outcome. CMS implies that pay-over-time contracts would be acceptable only if it is tied to an outcomes-based or evidence-based metric. These have been negotiated for individual drugs in certain Medicaid programs. But their adoption is not robust. With this in mind, we recommend that CMS consider expanding its view on VBPs beyond just the proposals outlined in the rule. Pay-over-time arrangements have many advantages for certain types of therapies, but face implementation barriers under the Medicaid program.

#### *Average Manufacturer’s Price (AMP)*

In addition to the changes in definition of VBP, CMS should consider changes in AMP to ensure pay-over-time arrangements are adopted. For instance, the proposed Best Price scheme in this rule is unlikely to be applicable since these agreements are unlikely to have different “prices,” but rather, a single price spread across several years. We recommend that CMS consider a reinterpretation of the Average Manufacturers Price to ensure these types of payment models are fully realized. In particular, CMS should allow manufacturers to reasonably interpret the AMP definition such that the total price of a product may be reflected in AMP at the time of sale—as opposed to just the initial installment payment, with subsequent installment payments reflected in AMP when they occur. In the case of value-based payment-over-time arrangements, if remaining installment payments do not come due because of the failure of the unit, manufacturers may treat these forgiven installment payments as a lagged price concession under the AMP smoothing methodology.

Regardless of the methodology, we recommend CMS consider allowing additional types of innovative payment models such as pay-over-time, if not



through finalization of this rule, then in future rulemaking, as a way to facilitate interim progress while not stymying discussion on future VBP evolutions.

### *Anti-kickback Statute*

As the Agency notes in the Proposed Rule's preamble, these nascent public payer arrangements have been important advances in value-based contracting as they have demonstrated an interest on the part of States to utilize alternative payment models to balance patient access and healthcare system sustainability. However, they have been the exception rather than the norm. Manufacturers' concerns about establishing an artificially skewed Best Price resulting from a rebate on a patient failure, or possibly running afoul of the Federal Anti-Kickback Statute (AKS), have hindered more widespread adoption of VBP arrangements in both the commercial and public markets.

Since 2016 the Agency has at least recognized the inflexibility of many public program payment rules in hampering development of alternative arrangements, and CMS has even encouraged industry to provide specific proposals for consideration.<sup>8</sup> Thus, this VBP proposal offers an important step forward, which we strongly support, but it requires additional clarity from both CMS and OIG to ensure it is useful broadly. While CMS indicates that this VBP proposal is not intended to "contradict any OIG guidance," it is hard to ignore the fact that the AKS remains a significant obstacle. For example, just last year OIG expressed concerns about the use of VBP arrangements with respect to drugs and certain devices when deciding only to extend new safe harbor protection to the medical care side of value-based care.<sup>9</sup>

BIO and many of our members provided significant commentary to OIG regarding this decision not to extend safe harbor protection to arrangements involving value-based arrangements for medicines, and we have in many cases in the past provided suggestions to OIG regarding the interplay of safe harbors and VBPs.<sup>10</sup> To that end, we viewed OIG's acknowledgement in 2019 that separate rulemaking was forthcoming to capture VBP arrangements involving drug

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<sup>8</sup> Medicaid Drug Rebate Program Notice for State Technical Contacts, Release No. 176 (July 14, 2016), at <https://www.medicaid.gov/medicaid-chip-program-information/by-topics/prescription-drugs/downloads/rx-releases/state-releases/state-rel-176.pdf>

<sup>9</sup> U.S. Department of Health and Human Services, Office of Inspector General; Proposed rule; "Medicare and State Healthcare Programs: Fraud and Abuse; Revisions To Safe Harbors Under the Anti-Kickback Statute, and Civil Monetary Penalty Rules Regarding Beneficiary Inducements," 84 Fed. Reg. 55,694 (October 17, 2019)

<sup>10</sup> See, e.g., BIO, Comment Letter on OIG Solicitation of New Safe Harbors and Special Fraud Alerts (Feb. 26, 2018), <https://www.regulations.gov/document?D=HHSIG-2018-0001-0005>; BIO, Comment Letter on HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs (Jul. 13, 2018), <https://www.regulations.gov/document?D=CMS-2018-0075-2634>; BIO, Comment Letter on OIG Request for Information Regarding the Anti-Kickback Statute and Beneficiary Inducements CMP (Oct. 26, 2018), <https://www.regulations.gov/document?D=HHSIG-2018-0002-0283>; BIO, Comment Letter on OIG Proposed Rule to Remove Safe Harbor Protection for Rebates Involving Prescription Pharmaceuticals and Create New Safe Harbor Protection for Certain Point-of-Sale Reductions in Price on Prescription Pharmaceuticals and Certain PBM Service Fees (Apr. 8, 2019), <https://www.regulations.gov/document?D=HHSIG-2019-0001-19736>.

manufacturers as a positive development. Yet, to date, further guidance has not been proposed. Accordingly, we view the current Proposed Rule as only a partial step forward absent enhanced guidance regarding these AKS considerations. Indeed, in some cases it may hinder programs aimed at the success of VBPs. For chronic therapies, VBPs tied to the outcomes can only be effective if patients adhere to their prescribed regimen. Nevertheless, certain adherence programs could be interpreted as a “kickback” under the broadly worded statute.

### ***Decoupling the VBP Provisions from Other Sections of the Proposed Rule***

The VBP proposals are an important step forward, and we urge CMS to separate the VBP provisions from other concerning provisions in the rule, specifically patient assistance programs (copay accumulator), as well as the new definitions of line extension and “new formulation” (our detailed concerns are outlined below). This would afford CMS the opportunity to move forward with the VBP proposals, including the recommendations put forward in this letter, without finalizing problematic policies that would have a negative impact on patient access to innovative treatments. We strongly believe the VBP provisions should move forward after making our suggested clarifications in order to provide payers, especially Medicaid Agencies, and manufacturers with more ‘tools’ to implement VBP arrangements. These clarifications – which we have outlined above – include, but are not limited to, confirmation of the voluntary nature of these agreements and the definition of VBP, as well as the clarification of Best Price in relation to ASP and AMP. Furthermore, additional operational challenges with VBPs detailed above could be resolved in future rulemaking and guidance. These include but are not limited to: the establishment of infrastructure between Medicaid and Government pricing systems, as well as appropriate IT systems; updated CMS and State Medicaid processes; 340B rulemaking and guidance; and, OIG guidance regarding the AKS.

### ***Exclusion of Certain Manufacturer Sponsored Patient Assistance Programs (“PBM Accumulator Programs”) From Determination of Best Price (§447.505) and Average Manufacturer Price (AMP) (§447.504)***

In the preamble to the Proposed Rule (85 Fed. Reg at 37298), CMS proposes significant changes to the treatment of manufacturer assistance programs and their current exclusion from Best Price and AMP reporting. Today, CMS notes, manufacturers make reasonable assumptions that discounts and other assistance to eligible patients through their patient assistance programs are generally excludable from these reporting requirements, because they meet established exemptions that apply to such programs when the full value of the discount or copay assistance is passed on to the patient (and some other entity in the supply chain does not receive any price concession).

However, CMS suggests that the growing popularity of so-called copay accumulator and maximizer programs has led to questions about whether these established exemptions continue to apply. In essence, these pharmacy benefit

manager (PBM)-developed programs exclude the value of copay assistance from accruing towards patient deductibles and annual cost sharing limits. According to the Proposed Rule, PBMs take the position that “manufacturer-sponsored assistance programs steer consumers towards more expensive medications when there may be more cost saving options available to health plans,” and, as a result, they force (“encourage”) health plans to apply manufacturer patient assistance programs to the benefit of the plan, instead of to the benefit of patients.<sup>11</sup> These arrangements are purportedly justified by PBMs as a cost control measure. However, the advent of these programs has caused significant confusion, higher out-of-pocket costs, and access issues for patients who rely on manufacturer assistance to meet their plan-imposed cost sharing obligations. Furthermore, our members offer these programs for innovative, medically necessary products for which there are often no alternatives available. Unfortunately, CMS recently finalized regulations which will lead to further expansion of these harmful programs, leaving use of these programs at the sole discretion of health plans and PBMs.<sup>12</sup>

To address the rise of copay accumulator and maximizer programs (which its own regulations have helped facilitate), CMS here proposes to revise exclusions from Best Price and AMP such that manufacturers could only exclude the amounts of patient assistance programs from the calculation of Best Price and AMP if they “ensure” the full value of the assistance is received by the patient.

**BIO strongly opposes CMS’s proposed revisions to the Best Price and AMP exclusions for copay assistance programs. These proposed revisions are based on incorrect factual assumptions, have no basis in the MDRP statute, and could not be operationalized even if finalized. Moreover, these changes would harm patients by undermining a critical pathway for access to medicines while increasing their out-of-pocket costs. Accordingly, we recommend CMS abandon this proposal.**

#### *Inconsistent with the MDRP Statute*

The Social Security Act defines Best Price to mean, “with respect to a single source drug or innovator multiple source drug of a manufacturer (including the lowest price available to any entity for any such drug of a manufacturer that is sold under a new drug application approved under section 505(c) of the Federal Food, Drug and Cosmetic Act), the lowest price **available from the manufacturer** during the rebate period **to any** wholesaler, retailer, **provider, health maintenance organization**, non-profit entity, or governmental entity within the United States,” subject to certain express exclusions.<sup>13</sup>

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<sup>11</sup> 85 Fed. Reg. at 37,289 & 37,298-99.

<sup>12</sup> See 85 FR 29164, “Patient Protection and Affordable Care Act; HHS Notice of Benefit and Payment Parameters for 2021; Notice Requirement for Non-Federal Governmental Plans,” May 14, 2020. Finalized language at 45 CFR §156.130 (cost-sharing requirements) permitted issuers to exclude amounts from manufacturer assistance programs from accruing toward cost sharing obligations.

<sup>13</sup> 42 U.S.C. § 1396r-8(c)(1)(C)(i) (bold-face emphasis added).

Notably, the statute does not include “patients” within the list of entities to which a manufacturer makes a price available for purposes of determining Best Price.<sup>14</sup> Furthermore, manufacturers do not intend for copay assistance to be “made available” to anyone except the patient. Use of the language “price *available from the manufacturer . . . to* [a Best Price-eligible entity]” implies that a manufacturer must affirmatively offer the price (or discount) to the Best Price-eligible entity. However, CMS’s proposal effectively reads this concept out of the statute and proceeds to impose an unworkable standard on manufacturers – one that purports to hold manufacturers accountable for the independent and opaque decision-making by health plans (and their contracted PBMs) that are wholly inconsistent with the manufacturer intent that patients alone receive the benefit of the copay assistance.

Under long-standing CMS guidance, manufacturers have adopted reasonable assumptions to reflect their intent and understanding that, absent evidence or knowledge to the contrary, the full value of copay assistance was received by eligible patients and, therefore, could appropriately be excluded from Best Price and AMP. Manufacturers are entitled to rely on reasonable assumptions in determining Best Price, consistent with the intent of the statute and regulations.<sup>15</sup> CMS now proposes to limit manufacturers’ ability to make such assumptions with respect to manufacturer assistance programs, effectively presuming for Best Price purposes that manufacturer assistance intended solely for patients is “made available to” (i.e., affirmatively offered to) a health plan or other entity, unless manufacturers can “ensure” that the full value of the assistance is received by the patient. Such a presumption ignores manufacturers’ prerogative to decide whether they make prices (and discounts) “available to” particular Best Price-eligible entities, such as health plans, or, alternatively, whether such prices (and discounts) are “available to” patients (as is the case for manufacturer assistance programs).

### *Operational Infeasibility*

In addition, CMS’s proposal to reinterpret the “ensure” standard misunderstands how copay accumulators work, suggesting that manufacturers control when and how they are implemented. Manufacturers already “ensure” that copay assistance is clearly intended for and directed to patients by providing this benefit entirely to the patient. As a threshold matter, it would be a misunderstanding of health plan’s operations and accumulator programs to suggest, as CMS appears to do in the Proposed Rule, that manufacturers are in a position to know (much less determine or control) how a health plan accounts for copay assistance programs intended for a particular patient when a plan has implemented an accumulator adjustment program. In most cases, manufacturers have no visibility into whether a health plan has adopted an accumulator adjustment program.

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<sup>14</sup> See 81 FR 5170, 5254, “Medicaid Program; Covered Outpatient Drugs; Final Rule,” Feb. 1, 2016. CMS stated in the preamble to the final rule that “patients are not one of the entities described in the statutory definition of Best Price . . .”

<sup>15</sup> See National Drug Rebate Agreement at §II.i.

Even if a manufacturer had cause to suspect copay assistance funds were being appropriated by a health plan pursuant to an accumulator program, manufacturers would face considerable challenges in investigating – on a plan-by-plan basis – such a suspicion, since plans are not required to publicly disclose (and often do not disclose) their policies accounting for copay assistance. At best, they are sometimes described in patient-facing plan documents, however these documents lack specificity and are subject to change.

This proposal is simply unworkable and will inevitably have a chilling effect on whether manufacturers offer such access programs in the future. Moreover, assuming for the sake of argument that manufacturers are able to ascertain whether manufacturer assistance is passed on to a health plan (or other entity) pursuant to an accumulator program, we must underscore that *only health plans* can decide how to account for manufacturer assistance.

Ultimately, manufacturers do not have the ability to control PBM or health plan decisions in such a way that this proposed change could be operationalized in the way CMS envisions. CMS asserts that it is merely requiring manufacturers to ensure that their patient assistance programs are used for the benefit of patients and not other parties. But there is an irrational (and unexplained) disconnect between the agency's proposed policy (i.e., ensuring that the full value of manufacturer support is provided to patients) and the practical ability of manufacturers to gain visibility into or control how health plans are operated.<sup>16</sup>

### *Increasing Barriers to Patient Access*

In addition to the operational problems, and significant departure from statutory intent, CMS' proposal would undermine a critical pathway for patient access. The regulatory burdens associated with this proposal are amplified by CMS' decision to reverse its previous policy on copay accumulators and maximizers in the final Notice of Benefit and Payment Parameters for 2021 as being subject to state law. The practical implication of CMS' proposal here is that manufacturers would need to design assistance programs that addressed potentially countless variations of benefit designs and the variability of accumulators being applied to different products, all while having none of the visibility into specific benefit designs that CMS supposes.

We are deeply concerned about the impact an expansion of these programs will have on medication adherence and access. CMS itself in the proposed rule acknowledged that when health plans apply accumulator programs, it is "to the detriment of the patient or consumer, thus generating savings for the plan."<sup>17</sup>As we previously commented to CMS, policies such as those ultimately finalized in the Notice (and proposed here) run counter to the Administration's own goals of

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<sup>16</sup> See generally *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto Ins.*, 463 U.S. 29 at 43 (1983) (agency must articulate a "rational connection between the facts found and the choice made").

<sup>17</sup> 85 Fed Reg 37298 (June 19 2020)

reducing patient's out-of-pocket costs for prescription drugs. The Administration highlighted the impact of adherence in the "Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs" and provides a call to action to reduce costs.<sup>18</sup> Copay assistance programs do just that, especially at a time when health plans' cost sharing requirements continue to increase with growing use of deductibles and coinsurance in the commercial market.<sup>19</sup>

Thus, CMS's proposal, if finalized, would represent a strong disincentive for copay assistance programs to exist in the same scope and function as they do today – further enhancing barriers to patients accessing the medicines they need. For these reasons, CMS should not move forward with this proposal.

### **Definition of "Line Extension" and "New Formulation"**

BIO is strongly opposed to CMS' proposed definition of line extension, which is a significant departure from its previous position and Congressional intent. Broadening the definition of "line extension," with a new definition of "new formulation" will have a chilling effect on innovation. As BIO has indicated in previous comments to the proposed definition in 2016,<sup>20</sup> "line extension" is defined in very limited terms, as "a new formulation of the drug, such as an extended release formulation, but does not include an abuse-deterrent formulation of the drug (as determined by the Secretary), regardless of whether such abuse-deterrent formulation is an extended release formulation."<sup>21</sup> Both the plain language of the statute and the clear (and repeatedly documented) intent of this provision dictate that this language should be interpreted narrowly.

In the Proposed Rule, CMS proposes to include in the definition of a "new formulation" "any change to the drug, provided that the new formulation contains at least one active ingredient in common with the initial brand name listed drug". Examples of products that would be new formulations under the proposed definition include:

- Extended release formulations;
- Changes in dosage form, strength, route of administration, ingredients, pharmacodynamics, or pharmacokinetic properties;
- Changes in indication accompanied by marketing as a separately identifiable drug (for example, a different NDC); and
- Combination drugs, such as a drug that is a combination of two or more drugs or a drug that is a combination of a drug and a device.<sup>22</sup>

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<sup>18</sup> Department of Health and Human Services (HHS), *American Patients First – The Trump Administration Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs* 9 (May 2018), available at <https://www.hhs.gov/sites/default/files/AmericanPatientsFirst.pdf>

<sup>19</sup> Katie Devane, et al., IQVIA, *Patient Affordability Part One* (2018), <https://www.iqvia.com/locations/unitedstates/patient-affordability-part-one>.

<sup>20</sup> *Comments on Proposed Rule on Covered Outpatient Drugs*, BIO, April 1, 2016.

<sup>21</sup> *Affordable Care Act* § 2502(d)

<sup>22</sup> *See id.*

This proposal is a vastly broader conception of “new formulation” than is currently understood or that was envisioned by Congress. If this proposal is adopted, every new strength of an oral solid drug would constitute a line extension subject to the alternative URA, as would new products that share but one active ingredient with an existing oral solid drug. Currently, approval of a new strength provides the basis for an independent price reporting stream.<sup>23</sup> CMS’s proposal would effectively tie inflation penalty rebate liability across strengths by operation of the alternative URA requirement.

Changes in a drug’s strength or dosage form on their own are not considered changes in how a drug is actually formulated. Indeed, as CMS itself has previously recognized, “if the only change to a drug is the strength, without any change to the formulation of the drug, section 1927(c)(2)(C) of the Act does not contemplate that a new strength is a line extension drug.”<sup>24</sup> Further, the statute specifically calls for separate price reporting streams for each “dosage form and strength” of a drug.<sup>25</sup> The statute refers to calculating “[t]he amount of the rebate . . . , with respect to each dosage form and strength of a single source drug or an innovator multiple source drug . . . ”<sup>26</sup> (referring to the rebate “with respect to each dosage and strength” of a drug). If Congress’s intent in creating the alternative URA provision were to subject all new strengths or dosage forms to the inflation penalties of predecessor products, it could have done so directly by changing these provisions of the statute. It did not. Instead, the statute contemplates that the amount of “average manufacturer price” would be different for each dosage form and strength of a drug.<sup>27</sup> The statute also specifies a “maximum rebate amount” that shall apply “with respect to each dosage form and strength” of a drug.<sup>28</sup>

Similarly, rebate liability for a combination product or a new product with a new indication—even if it has a separate NDA—could be tied to a preexisting product’s inflation penalty rebate under this proposed definition.<sup>29</sup> For the reasons described below, combination products and new indications are not new formulations and thus cannot be considered “line extensions” in any definition developed for purposes of the Alternative URA.

Combination drug products, particularly those that have new molecules and different approved indications, are new innovations that require extensive research and investment from the manufacturer. As such, they are not a “new formulation” of a drug, as required by the statute. Combination products represent the development of a new drug product through significant scientific and clinical

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<sup>23</sup> Proposed Rule at 37295.

<sup>24</sup> Final Rule, Medicaid Program; Covered Outpatient Drugs, 81 Fed. Reg. 5170, 5267 (2016).

<sup>25</sup> See *Williams v. Taylor*, 529 U.S. 362, 404 (2000) (noting “cardinal principle of statutory construction” that courts “must give effect, if possible, to every clause and word of a statute”)

<sup>26</sup> 42 U.S.C. § 1396r-8(c)(2)(A) (emphasis added); see also *id.* § 1396r-8(c)(1)(A)

<sup>27</sup> *id.* § 1396r-8(c)(2)(A)(ii)

<sup>28</sup> *id.* § 1396r-8(c)(2)(D)

<sup>29</sup> K&S Client Alert.

research. CMS itself acknowledged in its 2016 Proposed Rule that a Chemical Type 4 (new combination) product represents “a drug comprised of two or more components that are *physically, chemically, or otherwise combined or mixed to produce a single drug product.*”<sup>30</sup> The outcome of this combining or mixing is not a “new formulation” of the active ingredients of already-existing drug as CMS suggested. Combination drugs instead represent a *new product* to treat patients in different and innovative ways. Moreover, there are many different types of combination products. In other words, this term is not a “one size fits all.” For example, a combination product may be comprised of two previously unapproved active ingredients, one previously unapproved and one approved, or two previously approved active ingredients. In all cases, however, the successful development of a combination drug product can be expected to require significant research and development.

The statutory formula for calculating the Alternative URA, also confirms that the Alternative URA formula cannot be applied to combination drugs. Specifically, the statute provides that the manufacturer is to compare the total URA for the new formulation product, as calculated under section 1927(c) to the “highest additional rebate . . . under this section for any strength of the original single source drug or innovator multiple source drug.”<sup>31</sup> This language refers to the original drug in the singular only, and does not even recognize the possibility of there being more than one original drug to consider, as must be the case with a combination therapy. This statutory language makes clear that Congress could not have intended the Alternative URA calculation to apply to combination products and further demonstrates that there is no legal basis for CMS’ effort to extend the definition of “line extension” to combination products.

New indications “marketed as a separately identifiable drug product” also cannot qualify as “line extensions.” As described further below, obtaining approval for new indications of existing therapies can require significant investments in research and development, including new clinical studies. Doing so often provides important new treatment options to patients, including those for whom there are few or no other treatment options. Indeed, FDA has reported that “many important advances in drug therapy ... use an already FDA-approved drug to treat a new disease beyond that for which it was originally approved or to treat a new population of patients, such as children.”<sup>32</sup> Such advancements are not the type of “slight alteration” that Congress envisioned when it created the line extension provision. As we have noted in previous comments<sup>33</sup>, we believe CMS should identify as “line extensions” only those new dosage forms that do not require clinical investigations (other than bioavailability studies) for approval. FDA requires clinical investigations for product changes that may affect the safety and effectiveness of a product. Notably, FDA

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<sup>30</sup> 77 Fed. Reg. at 5339 (emphasis added).

<sup>31</sup> Social Security Act § 1927(c)(2)(C)(1)(II).

<sup>32</sup> CDER, New Drug Therapy Approvals 2019 (Jan. 2020), available at <https://www.fda.gov/media/134493/download>.

<sup>33</sup> *Comments on Proposed Rule on Covered Outpatient Drugs*, BIO, April 1, 2016.



does not generally consider changes in formulation, such as dosage form, to constitute that type of significant change. Because significant changes require clinical investigations beyond bioavailability studies, we believe that such changes are outside the scope of what may be appropriately considered a “line extension.”

Not only are CMS’ proposed new definitions inconsistent with the statute but, if adopted would provide disincentives to a manufacturer for investing in research for diseases that often have unmet needs. Pharmaceutical innovation is an extremely costly endeavor, and the treatment of drugs on the market is a serious consideration for manufacturers as they determine how to allocate limited resource dollars. If manufacturers decide the cost barriers resulting from the alternative rebate are too high, this could have the effect of hindering future innovation into new diseases, particularly rare diseases.

For example, CMS’ proposed rule could disincentivize investment in researching and obtaining approval for new indications for cancer therapies. Today, up to 35% of the oncology pipeline consists of oral anti-cancer medications (which are potentially subject to CMS’ proposed line extension definition).<sup>34</sup> The manufacturers of these therapies frequently devote significant resources to expanding these therapies to new patient populations. For example, FDA first approved COMETRIQ® (cabozantinib) in 2012 for a small number of patients with a rare thyroid cancer. In the years that followed, phase 3 registrational cabozantinib clinical trials failed in prostate cancer, forcing the manufacturer to restrict spending, reduce its workforce by more than 70 percent, and focus its limited resources and financial reserves to study cabozantinib in kidney and liver cancer. Clinical trials ultimately demonstrated positive results, and FDA approved CABOMETYX™ (cabozantinib) for these indications in 2016. This example demonstrates the significant financial risks manufacturers take on to seek FDA approval for new indications. CMS should not dilute incentives for manufacturers to take on such risks — to the ultimate detriment of patients — by treating the resulting innovations as the type of “slight alteration” that constitutes a line extension.

In addition, BIO urges CMS to clarify the meaning of “corporate relationship” that it uses in the preamble to indicate that a manufacturer that has a “corporate relationship” with the original manufacturer of a product would be required to use the Alternate URA. This could be interpreted in multiple ways, but a liberal interpretation would imply that a separate entity that has a business relationship with the original manufacturer that has done its own clinical research and development might still be required to use the Alternate URA. We ask CMS to confirm this is not the case by defining “corporate relationship.”

Furthermore, these new definitions would stymie research into new, innovative means of administering the drug that could help patients who are unable to take a drug in the original manner. Innovative research into new types of administration can ensure all patients that need the drug therapy can access that therapy. CMS

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<sup>34</sup> Mosely WG, Nystrom JS. Dispensing oral medications: why now and how, *Community Oncology*. 2009; 6:358-61.

should not create barriers to study and advancement of new means of drug therapy administration.

Moreover, stifling innovative therapies can also produce negative economic impacts; resulting in increased spending across the healthcare eco-system. Conversely, innovative therapies that promote medication adherence prevent unnecessary episodes of care and thus, provide financial savings to our nation's health care systems. For example, among Medicaid patients with chronic diseases such as cardiovascular disease, diabetes, respiratory diseases (asthma/chronic obstructive pulmonary disease), and serious mental health conditions (depression and schizophrenia/bipolar disorder) improving medication adherence could produce \$8 billion in savings annually.<sup>35</sup>

Therefore, BIO strongly urges CMS not to finalize such a broad definition that is inconsistent with statute in such a way that it will disincentivize development of new, innovative therapies. Notwithstanding our concerns, if CMS does finalize a definition of "line extension" and "new formulation," CMS should confirm that any new regulation defining the terms should be prospective from the date of implementation. Manufacturers that relied upon "reasonable assumptions" in good faith to identify line extension products should not be subject to costly retrospective changes. We note that retroactivity is not favored in the law, and a "grant of legislative rulemaking authority will not . . . be understood to encompass the power to promulgate retroactive rules unless that power is conveyed by Congress in express terms."<sup>36</sup>

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Thank you for the opportunity to comment on this proposed rule. BIO looks forward to working with CMS to advance the VBP provisions and we strongly urge CMS to withdraw its problematic proposals regarding line extension and copay assistance, which will harm patient access to innovative therapies. Please feel free to contact us if you have any questions regarding our comments.

Sincerely,

/s/

and

/s/

Crystal Kuntz  
Vice President,  
Healthcare Policy and Research

Jack Geisser  
Senior Director  
Healthcare Policy,  
Medicaid, and State  
Initiatives

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<sup>35</sup> Roebuck, Mark C., Robert J. Kaestner, and Julia S. Dougherty. "Impact of Medication Adherence on Health Services Utilization in Medicaid." *Medical care* 56.3 (2018): 266-273.

<sup>36</sup> See, e.g., *Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 208 (1988)