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VIA ELECTRONIC FILING — *http://www.regulations.gov*

Seema Verma
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
7500 Security Boulevard
Baltimore MD 21244-8016
Attn: PO Box 8016

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

Dear Administrator Verma:

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to submit comments on the above-referenced Medicaid proposed rule published by the Centers for Medicare & Medicaid Services (CMS) at the U.S. Department of Health and Human Services (HHS).[1] PhRMA is a voluntary, non-profit organization representing the country's leading research-based pharmaceutical and biotechnology companies. PhRMA members are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives.

America's biopharmaceutical companies are committed to developing solutions to help diagnose and treat those with COVID-19, a disease caused by a novel strain of coronavirus. In addition to applying their scientific expertise to find ways to diagnose, treat, and prevent infections from the virus, the biopharmaceutical industry is providing financial support and in-kind donations to organizations and collaborating with U.S. and global health authorities to combat this global public health emergency. Most PhRMA members have research and development efforts underway and are providing donations of medicines and critical medical supplies to support patients and first responders in addressing this evolving crisis.

The proposed rule addresses many topics of great importance both to Medicaid and to our country's health care system generally. Several of these issues, in fact, could have a central role in shaping the future course of our health care system. Moreover, these proposals could have widespread impacts on the biopharmaceutical marketplace, as they focus on or have repercussions for several government pricing metrics (Medicaid rebate metrics and the Medicaid

[1] 85 Fed. Reg. 37,286 (June 19, 2020).

unit rebate amount (URA),the 340B Program ceiling price, and Medicare Part B drug payments). As a result, we are concerned that CMS packaged these issues into one proposed rule with a 30-day comment period, which denies commenters adequate time and opportunity to prepare comments on these issues. Nevertheless, PhRMA and its members have worked continually over this brief period to prepare comments. We hope CMS will take the time to consider them carefully.

Our comments on the key issues in the proposed rule can be summarized as follows:

- **Pharmacy benefit manager (PBM) and health plan accumulator adjustment programs**.[2] CMS proposes that manufacturer patient assistance programs be included in best price and average manufacturer price (AMP) unless manufacturers "ensure" that their assistance solely benefits patients and does not benefit third parties—such as through PBM and health plan "accumulator adjustment" schemes. This proposal is based solely on unexplained and unsupported assumptions about manufacturers' assistance programs—which already deliver assistance solely to patients—and on a clearly erroneous interpretation of the Medicaid rebate statute's best price provision. The statute's plain language provides that best price includes only "price[s] available from the manufacturer . . . to [a specific best price-eligible customer]." While CMS considers health plans to be best price-eligible customers, patients are not best-price eligible. A manufacturer does not make a "price available" to a health plan when a plan unilaterally undertakes efforts to deny patients the benefit of assistance that the manufacturer designed only for, and delivered only to, patients. Moreover, this proposal is not based on reasoned decision-making, and it could lead to patients paying more out of pocket for medicines, which is an especially poor policy choice during a nationwide public health emergency accompanied by steep economic pain for millions of patients. Accordingly, PhRMA strongly opposes CMS' proposal, and CMS must not finalize this proposal.

- **Line extensions**. PhRMA strongly opposes CMS' proposed definition of a "line extension" subject to higher Medicaid rebates, which exceeds CMS' legal authority and must not be finalized. CMS' sweeping proposal goes far beyond the authority granted to CMS in the statutory provision on line extensions, which establishes narrow and well-defined bounds on the types of changes in an existing drug that can be classified as "line extensions;" conflicts with U.S. Food and Drug Administration (FDA) regulations and policies designed to promote public health; and cuts at the heart of continued pharmaceutical innovation. If finalized, the proposal would create serious financial penalties for manufacturers seeking to improve their products based on continually evolving research and science and risks impeding progress in patient care at a time when pharmaceutical innovation is more important than ever.

- **Value-based arrangements**. PhRMA and its member companies strongly support value- based arrangements, which align payments for biopharmaceutical

[2] The proposed rule uses the term "PBM accumulator programs," but they are, in fact, the opposite, because plans and PBMs refuse to accrue the value of assistance designed to help patients.

products with their value and thus promote CMS' volume to value initiative in the biopharmaceutical arena. Given the substantial benefits that these arrangements can create, we greatly appreciate CMS' efforts to facilitate value-based arrangements throughout this proposed rule. Specifically, we support CMS' proposals regarding the recognition of value-based arrangements as bundled sales; support the proposal to permit restatements of value-based arrangements for periods exceeding 12 quarters with certain clarifications; and offer suggestions on CMS' proposed definition of "value-based purchasing (VBP) arrangement." We are unable to offer substantial comments on the proposed rule's "multiple best prices" proposal, as this section of the proposed rule lacks sufficient information for us to understand the multiple best price approach and formulate informed comments; therefore, we ask CMS not to finalize the multiple best price proposal and instead to promulgate another proposed rule with additional information that fleshes out the multiple best price concept and enables stakeholders to develop meaningful comments on this approach.

- **State-related proposals**. With regard to CMS' state-focused proposals, PhRMA requests that CMS revise the definition of "CMS-authorized supplemental rebate agreement" to clarify that a supplemental rebate agreement may be approved by CMS as long as the combined rebate payment under the supplemental and national rebate agreements is greater than or equal to the rebate under the national rebate agreement alone. PhRMA also requests that CMS reinforce the need for states to file state plan amendments prior to implementing changes to supplemental rebate agreements, as CMS has raised in the proposed rule. PhRMA supports CMS' goal of improving the integrity of data reported to states under the Medicaid Drug Rebate Program (MDRP), but requests that CMS also mandate that states provide claims-level data as a means of ensuring the accuracy of their calculations and reporting. PhRMA further requests that CMS works directly with states to ensure that value-based arrangement reporting only includes reasonable data elements and complies with confidentiality obligations set forth in the MDRP statute at section 1927(b)(3)(D) and that states work with manufacturers to ensure the accuracy of information on value-based arrangements that is submitted to CMS.

- **New Medicaid Drug Utilization Review (DUR) provisions designed to reduce opioid-related fraud, misuse, and abuse**. As required by the SUPPORT for Patients and Communities Act (SUPPORT Act), CMS is proposing minimum standards for opioid-related DUR programs to ensure a minimum baseline of activities in the states. Additionally, CMS is codifying SUPPORT Act requirements that states implement programs to monitor concurrent use of opioids with benzodiazepines as well as with antipsychotics, requirements for states to establish processes to identify fraud and abuse of controlled substances, and programs to manage appropriate use of antipsychotic medication in children. CMS is also taking additional steps to establish and encourage minimum safety standards for Medicaid DUR programs beyond SUPPORT Act requirements. We support CMS' efforts to curb inappropriate and potentially unsafe utilization of prescription medicines while also ensuring not to impede patients' access to

medically necessary drugs, particularly for vulnerable populations with complex and chronic health conditions.

Our detailed comments follow below.

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A. PBM and Health Plan Accumulator Adjustment Programs

CMS' proposed changes related to patient assistance are contrary to the Medicaid rebate statute and are based on faulty and unsupported assumptions about manufacturer patient assistance programs. If finalized, these changes could potentially reduce the availability of patient assistance, which could, in turn, inhibit the ability of patients to pay their out-of-pocket costs. As a result, these proposed changes could lead to patient abandonment of necessary therapies and could worsen health outcomes.

CMS proposes to require manufacturers to include discounts and assistance to patients in their calculation of best price unless manufacturers "ensure" that this assistance solely benefits patients and does not benefit third parties. CMS argues that the proposed changes are necessary in light of health plans'[3] and PBMs' increasing use of accumulator adjustment programs.[4] This proposal could impact a broad range of manufacturer-sponsored patient assistance currently exempt from best price, including coupons, drug discount card programs, patient refund/rebate programs, and copay assistance programs. The proposed changes could also potentially affect a broad variety of drug pricing metrics beyond even best price, which could cause turbulence throughout the biopharmaceutical marketplace. For the reasons set forth below, PhRMA strongly urges CMS not to finalize this proposal.

1. Manufacturer Patient Assistance Programs Are Designed to Benefit Patients, While Accumulator Adjustment Programs Harm Patients

Patient assistance programs provide an important source of financial support for eligible patients and can improve patient adherence, leading to improved patient outcomes. When patients' cost-sharing obligations rise, patients are more likely to abandon their medicines. In 2017, 69 percent of commercially insured patients did not fill their new prescriptions when they had to pay more than $250 out of pocket, while only about 11 percent of patients with out-of-pocket costs of less than $30 abandoned their prescriptions at the pharmacy.[5] Thus, higher patient out-of-pocket costs frequently lead to medicines that have been prescribed by a health care provider—and that a health plan has agreed to cover—never reaching the patient because the patient's health plan has erected a financial barrier around appropriate treatment. Troublingly, the out-of-pocket burden for patients is growing because of rapidly increasing patient cost sharing for brand medicines, a result of commercial market health plans and PBMs

[3] CMS has defined "provider" in a way that encompasses health plans and therefore considers health plans to be best price-eligible entities. CMS adopted this definition in its 2016 rule even though this is not a plain language concept of a "provider."

[4] 85 Fed. Reg. 37,286, 37,289 (June 19, 2020).

[5] Katie Devane, et al., Patient Affordability Part Two: Implications for Patient Behavior & Therapy Consumption, IQVIA (2018), available at https://www.iqvia.com/locations/united-states/library/case-studies/patient-affordability-part-two.

increasing reliance on large deductibles and coinsurance.[6] For these reasons, CMS has recognized the importance of patient assistance, noting that it is crucial for "consumers whose drug costs would otherwise be extremely high due to a rare or costly condition."[7]

Cost-sharing assistance is an important protection for patients to help them access and adhere to prescribed medications that both prescribers and plans agree are appropriate.[8] Because commercial health plans have increasingly shifted the burden of prescription drug costs to patients, high-cost ($125+) drug claims accounted for over 50 percent of total patient cost exposure in 2017, a 20 percent increase from 2013.[9] As coverage for medicines has eroded and left patients facing higher cost sharing, manufacturer cost-sharing assistance has come to play a critical role in improving patient affordability. For example, in 2019, 70 percent of patients taking brand medicines to treat multiple sclerosis (MS) used cost-sharing assistance to help them pay the high out-of-pocket costs set by their plan. Without cost-sharing assistance, these patients would have paid over five times more out of pocket ($2,238 more, on average).[10] Similarly, patients taking brand diabetes medicines would have paid more than twice as much out of pocket if they were prevented from using cost-sharing assistance.[11]

Multiple studies report that manufacturer cost-sharing assistance is associated with higher adherence and lower rates of therapy discontinuation.[12] For patients at risk of

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[6] Katie Devane, et al., Patient Affordability Part One: The Implications of Changing Benefit-Designs and High Cost-Sharing, IQVIA (2018), available at https://www.iqvia.com/locations/united-states/library/case-studies/patient-affordability-part-one; Tracking the Rise in Premium Contributions and Cost-sharing for Families with Large Employer Coverage, Peterson-Kaiser Family Foundation (August 2019), available at https://www.healthsystemtracker.org/brief/tracking-the-rise-in-premium-contributions-and-cost-sharing-for-families-with-large-employer-coverage/ (showing a 205 percent increase in commercial market enrollee spending on deductibles from 2007 to 2017, vastly outpacing wage growth); Trends in Specialty Drug Benefits Report, 2017 Edition, Pharmacy Benefit Management Institute (2017), available at https://www.pbmi.com/ItemDetail?iProductCode=SPECIALTY_2017&Category=SPECIALTY (noting that, in 2016, coinsurance overtook copays as the preferred form of cost sharing on commercial plans for specialty drugs).

[7] 84 Fed. Reg. 17,454, 17,544 (Apr. 25, 2019).

[8] Plans and PBMs have a wide array of tools available to manage the pharmacy benefit in order to control costs, including utilization management techniques such as drug exclusion lists, prior authorization, and step therapy. Data show that these tools are well utilized, with 95 percent of employers using prior authorization and 86 percent using step therapy. Trends in Specialty Benefit Report, 2019 Edition, Pharmacy Benefit Management Institute (2019), available at https://www.pbmi.com/ItemDetail?iProductCode=SPECIALTY_2019&Category=SPECIALTY.

[9] Katie Devane, et al., Patient Affordability Part One: The Implications of Changing Benefit-Designs and High Cost-Sharing, IQVIA (2018), available at https://www.iqvia.com/locations/united-states/library/case-studies/patient-affordability-part-one.

[10] IQVIA Analysis for PhRMA. U.S. Market Access Strategy Consulting Analysis (2020).

[11] Id.

[12] See, e.g., Jonas B. Daugherty, et al., The Impact of Manufacturer Coupon Use in the Statin Market, 19 J. Managed Care & Specialty Pharmacy 765 (2013); Matthew Daubresse, et al., Effect of Prescription Drug Coupons on Statin Utilization and Expenditures: A Retrospective Cohort Study, 27 Pharmacotherapy 12 (2017).

prescription drug abandonment due to high cost sharing, another study found that cost-sharing assistance typically reduced patients' monthly out-of-pocket costs to a level where they were much less likely to abandon therapy.[13] CMS itself has acknowledged that "copayment support may help beneficiaries by encouraging adherence to existing medication regimens, particularly when copayments may be unaffordable to many patients."[14]

While patient assistance programs benefit patients, accumulator adjustment programs harm patients. Ignoring harms to patient adherence and well-being, health plans and PBMs continue to institute these programs, under which patients are punished for using cost-sharing assistance and end up paying more out-of-pocket than their plans would otherwise permit. Accumulator adjustment programs can potentially leave patients with thousands of dollars in unexpected costs at the pharmacy, resulting in exactly the problems that cost-sharing assistance is designed to avoid: prescription abandonment, poor health outcomes, and unnecessary medical spending. If patients cannot pay their full cost sharing at the pharmacy, they are typically turned away and leave the pharmacy without the medicine their doctor prescribed. For example, researchers have found that—after the implementation of an accumulator adjustment program—high deductible health plan enrollees taking autoimmune specialty drugs had a 20 percent higher level of treatment discontinuation.[15] As an AIDS Institute report on accumulator adjustment programs reported: "Copay accumulator programs put patients with chronic conditions in a tough position—forcing them to choose between their health and other financial obligations."[16]

Accumulator adjustment programs can increase patient out-of-pocket spending, reduce adherence, and result in poor health outcomes. It therefore comes as no surprise that manufacturers have consistently opposed accumulator adjustment programs. In past comments, PhRMA has explained that these programs "penalize patients for using cost-sharing support and force them to pay more out of pocket than is ordinarily permitted under their plans, adversely impacting medication adherence and patient health."[17] In comments to the 2020 Notice of Benefit and Payment Parameters (NBPP) proposed rule, PhRMA urged CMS to make clear that "cost-sharing support for a brand drug on the formulary would always count toward the annual limitation on cost sharing" if no medically appropriate or affordable generic drug was available on the formulary.[18] Additionally, when CMS abruptly proposed to reverse its previous position

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[13] Catherine I. Starner, et al., Specialty Drug Coupons Lower Out-of-Pocket Costs and May Improve Adherence at the Risk of Increasing Premiums, 33 Health Affairs 1761 (2014).

[14] 84 Fed. Reg. 17,454, 17,544 (Apr. 25, 2019).

[15] Bruce W. Sherman, et al., Impact of a Co-pay Accumulator Adjustment Program on Specialty Drug Adherence, 25 Am. J. Managed Care 335 (2019).

[16] Copay Accumulator Adjustment Programs, AIDS Institute 5 (June 2020), available at http://www.theaidsinstitute.org/sites/default/files/attachments/AI_CoPay_Accumulator_Adjustment_Brochure_w%20Appendix_FINAL.pdf.

[17] PhRMA, Comments on Transparency in Coverage Rule, CMS-9915-P (Jan. 28, 2020), at 7.

[18] PhRMA, Comments on CMS-9926-P (Feb. 19, 2019), at 7. CMS finalized the 2020 NBPP proposed rule but then reversed course in the 2021 NBPP, potentially resulting in significant human costs. See Michelle Andrews, 2021 Health Plans Granted Leeway To Limit Consumers' Benefit From Drug Coupons, Kaiser Health News (July 6,
(continued…)

on accumulator adjustment programs in the 2021 NBPP proposed rule, PhRMA expressed "deep[] concern[]," explaining that the proposal would "result in higher prescription drug costs for millions of patients across the Nation."[19] In light of CMS' acknowledgment in this proposed rule that accumulator adjustment programs can harm patients by making them pay more out-of-pocket for a drug,[20] it is puzzling that CMS continues to promote policies—both in this proposed rule and the 2021 NBPP final rule—that benefit accumulator adjustment programs and could ultimately lead to higher out-of-pocket costs for patients.

2. The Proposed Changes Are Contrary to the Best Price Provision of the Medicaid Rebate Statute

CMS proposes to require manufacturers to "ensure" that the benefit of patient assistance programs goes entirely to patients. Manufacturers already ensure that the benefit of these programs goes entirely to patients by providing this assistance solely to patients. Further, requiring manufacturers to include in the calculation of best price the value of patient assistance provided by manufacturers to patients and subsequently taken away from patients by plans is contrary to the statutory definition of best price because patient assistance is not a price or a price concession that is available from a manufacturer to plans.

a. Because Manufacturers Provide Assistance Solely to Patients, Who Are Not Best Price-Eligible Entities, CMS' Proposed Rule Contravenes the Best Price Statute

In the proposed rule, CMS suggests that if an accumulator adjustment program is applied to manufacturer assistance provided to a patient, the manufacturer is somehow not "ensuring" that the full value of the assistance is passed onto the patient.[21] This is incorrect. At the point when a PBM or plan could apply an accumulator adjustment to manufacturer patient assistance, the manufacturer has already provided the assistance to the patient, thereby ensuring that the full value of the assistance is passed onto the patient. The benefit provided to patients through manufacturer cost-sharing assistance happens at the point of sale (helping the patient meet their point of sale cost sharing obligation). Any accumulator adjustment programs health plans may impose after-the-fact occur later, downstream from the point of sale, through benefit design/health plan business rules (for example, plan rules addressing how to the health plan will apply or not apply cost-sharing assistance toward a patient's deductible and maximum out-of-pocket obligation). However, the proposed rule preamble seems to miss this distinction and imply that a manufacturer's delivery of assistance to a patient is not enough to meet the proposed "ensure" standard. Rather, CMS may be seeking to extend a manufacturer's responsibility to ensure that the full value of patient assistance remains with the patient far into the future, when the manufacturer has already provided the assistance to patients, and someone else has control

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2020), available at https://khn.org/news/2021-health-plans-granted-leeway-to-limit-consumers-benefit-from-drug-coupons/.

[19] PhRMA, Comments on CMS-9916-P (Mar. 2, 2020), at 1.

[20] 85 Fed. Reg. 37,286, 37,298 (June 19, 2020).

[21] 85 Fed. Reg. 37,286, 37,299 (June 19, 2020).

over manufacturer-provided assistance. Placing such a requirement on manufacturers has no basis in logic or the law.

The proposed rule also suggests that manufacturers somehow allow or acquiesce in plans taking assistance away from patients, alluding vaguely to manufacturers failing to establish "parameters" or "coverage criteria" around their patient assistance programs. CMS does not explain what it means by these cryptic statements or provide any evidence to support them. Manufacturers do not intend to (and do not) provide any value to health plans through patient assistance programs, nor do they in any way acquiesce in these thefts of patient assistance. Rather, as discussed above, manufacturer assistance programs provide value to patients—and the plan, when using an accumulator adjustment program, then takes that assistance away from the patient. CMS has provided no evidence to support its suggestion that manufacturers may somehow acquiesce in this taking and thus (as explained further below) CMS has not met its burden under the Administrative Procedure Act to support assumptions underlying a rule with evidence in the record. In fact, CMS has not established any basis for concluding that benefits from manufacturer patient assistance programs go to anyone other than patients. Patients are not best price-eligible entities under the Medicaid rebate statute.[22] Under the statute, best price is determined based only on the prices "made available from" a manufacturer to "any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity within the United States."[23] CMS does not have the statutory authority to expand this list of best price-eligible entities via rulemaking, as it is attempting to do here.[24] Thus, this proposal exceeds CMS' statutory authority.

b. Because Patient Assistance Upon Which an Accumulator Adjustment Program Is Later Imposed Is Not a Price, CMS' Proposed Rule Contravenes the Best Price Statute

CMS also contradicts the Medicaid rebate statute because a plan's unilateral diversion of manufacturer assistance provided to a patient is not a "price" within the plain meaning of the statute. The best price statute requires manufacturers to include in their calculation of best price the "lowest price available from the manufacturer during the rebate period" to any best price-eligible entity.[25] Black's Law Dictionary defines "price" as "[t]he amount of money or other consideration asked for or given in exchange for something else; the cost at which something is bought or sold."[26] Manufacturer patient assistance programs do not affect either the "amount of money or other consideration asked for or given in exchange for" manufacturer products sold to best price-eligible entities or the "cost at which" manufacturers sell their products. Further, a plan cannot unilaterally change the "price" at which a

[22] 42 U.S.C. § 1396r-8(c)(1)(C).

[23] 42 U.S.C. § 1396r-8(c)(1)(C).

[24] Cuozzo Speed Techs., LLC v. Lee, 136 S. Ct. 2131, 2141-42 (2016) (noting that courts may invalidate "'shenanigans'" by an agency that are "outside [its] statutory limits"); Civil Aeronautics Bd v. Delta Air Lines, Inc., 367 U.S. 316, 328 (1961) (noting an agency's request for "power to do indirectly what it cannot do directly").

[25] 42 U.S.C. § 1396r-8(c)(1)(C).

[26] Price, Black's Law Dictionary (11th ed. 2019).

manufacturer sells its product by siphoning away manufacturer assistance provided to patients; such assistance only helps patients pay their out-of-pocket costs; it does not affect the price at which the drug is available from the manufacturer.[27]

This proposal is therefore "foreclosed by the plain language of the statute and the common understanding" of the word "price."[28] It is well-established that the plain language of a statute controls its meaning unless the meaning would be "absurd or glaringly unjust."[29] An interpretation that "price" means the "cost at which something is bought or sold"—*i.e.,* that price means price[30]—is neither "absurd nor glaringly unjust." If "the plain language of the statute unambiguously indicate[s] that Congress sought to foreclose" an agency action, the reasonableness of the action is not determinative.[31] The Medicaid drug rebate statute is clear that best price includes only "prices" available from a manufacturer. Any amounts that a plan may achieve by diverting manufacturer assistance intended for patients is not a "price" (nor, as explained below, is it "available from the manufacturer" to the plan). Thus, this proposal is contrary to the plain language of the best price provision of the Medicaid rebate statute.

c. Because Manufacturers Do Not Make Patient Assistance Available to Plans, CMS' Proposed Rule Contravenes the Best Price Statute

Additionally—and most importantly—the Medicaid rebate statute defines best price as the lowest price "available from the manufacturer … to" a best price-eligible entity.[32] A price is only "available from a manufacturer to" a specific party if the manufacturer intends to make the price available to that party. CMS has acknowledged the relevance of intent in determining whether a price is "available from" a manufacturer to a best-price eligible entity for best price purposes. For example, the best price regulation excludes from best price "PBM rebates, discounts, or other financial transactions" unless such transactions are "designed to adjust prices at the retail or provider level" (*i.e.,* unless the manufacturer intends the transaction to reduce prices to best price-eligible retailers or providers).[33] Similarly, in discussing patient assistance in the 2016 final rule on covered outpatient drugs, CMS states that "programs being excluded from AMP and best price [must be] programs that are designed to benefit or assist only the patient."[34]

In fact, Congress emphasized the intentional, negotiated nature of those prices that are included in best price in a 1991 report describing the key features of the recently-enacted rebate

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[27] Massachusetts v. Mylan Labs., 608 F.Supp.2d 127, 143 (D. Mass. 2008) (distinguishing "cost" and "price").

[28] See City of New York v. Comm'r Internal Revenue, 70 F.3d 142, 144 (D.C. Cir. 1995).

[29] United States v. Rodgers, 466 U.S. 475, 484 (1984).

[30] See U.S. ex rel. Streck v. Allergan, Inc., 894 F. Supp. 2d 584, 600 (E.D. Penn. 2012) (holding that it was reasonable to interpret "price paid to the manufacturer" under AMP as "just that, the price initially paid to the manufacturer by the wholesaler").

[31] Zuni Pub. Sch. Dist. No. 89 v. Dep't of Educ., 550 U.S. 81, 93-94 (2007).

[32] 42 U.S.C. § 1396r-8(c)(1)(C) (emphasis added).

[33] 42 C.F.R. § 447.505(c)(17) (emphasis added)

[34] 81 Fed. Reg. 5,170, 5,235 (Feb. 1, 2016) (emphasis added).

statute, explaining that the rebate statute "provides a vehicle for providing Medicaid programs with the same 'best price' discounts which other large-buying entities secured through negotiation."[35] The whole point of the best price provision is to extend to Medicaid the best of the prices the manufacturer has given to other (best price-eligible) customers.

Thus, a price is only "available from" a manufacturer to a best price-eligible entity if the manufacturer intends to offer the price to that entity.[36] Manufacturers do not intend to make the benefits of patient assistance programs available to plans. As explained above, manufacturers design their patient assistance programs to benefit patients, and these programs do benefit patients by helping them pay their out-of-pocket costs. A price "available from a manufacturer … to" a plan cannot logically be understood to refer to an amount obtained by a plan by unilaterally taking assistance the manufacturer intended for and provided to patients. Therefore, requiring a manufacturer to include such amounts in the calculation of best price contravenes the plain language of the Medicaid rebate statute.

Further, the way CMS seems to be construing its proposed regulatory language is a bizarre construction of the statute that would reward plans for misappropriating manufacturer assistance at the expense of patients who already pay premiums in exchange for prescription drug coverage. This would have the ridiculous effect of turning thefts into *price concessions to the thief*. Statutes must not only be interpreted in accordance with their plain language, they must also be interpreted to avoid absurd results.[37] The CMS proposed rule would violate both of these long-standing canons of statutory construction.

3. The Proposal Is Not a Product of Reasoned Decision-making

Even if this proposed change were consistent with the best price provision of the Medicaid rebate statute (which it is not), CMS could not finalize this proposal because it is based on assumptions that are not supported by the record (and in fact are contradicted by a multitude of contrary evidence in the record), and it fails to address the far-reaching impacts of the proposed changes on government price reporting and on patients.

In the proposed rule, CMS seems to assume that there is a channel of communication between manufacturers and health plans through which discussions about accumulator adjustment programs occur, or that somehow manufacturers otherwise allow or acquiesce in accumulator adjustment programs, suggesting in the rule's preamble that manufacturers can control accumulator adjustment programs by "monitor[ing] or plac[ing] parameters around how the benefits" of patient assistance programs are applied and "establish[ing] coverage criteria" for these program. Such a channel of communication does not

[35] H.R. Rep. 102-384(I) at 3 (1991) (emphasis added).

[36] For example, the court in a Robinson-Patman case held that "price" must be calculated by deducting from the base or invoice price "any discounts or offsets knowingly granted to a buyer," noting that "quantity discounts," "cash discounts based on time or mode of payment," and "rebates" all count toward price as they are "knowingly given by the supplier." Kapiolani Motors, Ltd. v. Gen. Motors Corp., 337 F. Supp. 102, 104 (D. Haw. 1972).

[37] See, e.g., Clinton v. City of New York, 524 U.S. 417, 429 (1998) ("the Government's new-found reading of [the disputed statute] 'would produce an absurd and unjust result which Congress could not have intended'") (quoting Griffin v. Oceanic Contractors, Inc., 458 U.S. 564, 574 (1982)).

exist.[38] The lack of manufacturer involvement with accumulator adjustment programs is evident from CMS' description of these programs in the preamble to the proposed rule. Specifically, CMS notes that health plans are "instructed or encouraged by their pharmacy benefit managers (PBMs)" to adopt accumulator adjustment programs, health plans implement these programs, and, pursuant to these programs, PBMs do not apply manufacturer patient assistance to a patient's deductible.[39] Missing from CMS' discussion of accumulator adjustment programs is the role of manufacturers—because manufacturers play no part in the development or implementation of these programs, and have no influence over their development or implementation. Which makes sense—these accumulator adjustment programs are designed to block manufacturers' own patient assistance programs; allowing these programs to operate would be a self-defeating step that would nullify the manufacturer's own programs.

Further, although manufacturers already ensure that the benefits of patient assistance programs go solely to patients by providing these benefits solely to patients, the proposed rule preamble suggests that CMS might see this as insufficient to "ensure" that the assistance is solely received by patients (even though this does not make sense), suggesting that manufacturers somehow are allowing accumulator adjustment programs to operate. The record is devoid of any support for these assumptions—upon which CMS has premised this entire proposal. CMS assumes—without explanation, and without any supporting evidence—that manufacturers somehow allow or acquiesce in plans using accumulator adjustment programs to take manufacturer assistance away from patients, that manufacturers can consistently identify when plans apply accumulator adjustment programs, and that manufacturers can prevent plans from applying these accumulator adjustment programs. But the Administrative Procedure Act requires that the facts upon which CMS relies for this rulemaking have "some basis" in the administrative record.[40] CMS is not entitled to rely on a "conclusory statement [that] is unsupported" by evidence in the record,[41] nor is it entitled to deference when promulgating a rule "without substantial basis in fact."[42]

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[38] See Upstream Reporting of Copay Assistance Issues Brief, Nat'l Council for Prescription Drug Programs 7 (June 2018), available at https://www.ncpdp.org/NCPDP/media/pdf/20180604_Upstream_Reporting_of_Copay_Assistance_Issues_Brief.pdf?ext=.pdf ("There is currently no standard mechanism to share transaction data between prescription assistance programs and commercial health insurance programs."). Even more troubling, "PBMs have intentionally tried to hide [a]ccumulator [a]djuster. . .programs from manufacturers and, in many cases, patients." Dave MacDougall, et al., Accumulating Risk: PBM Accumulator Adjuster Programs Already Hurt Gross-to-Net; Now CMS Wants to Count Them Against Medicaid Best Price, Hayden Consulting Group (July 2020). Despite this reality, CMS has ignored calls in the past to require health plans to be more transparent about their use of accumulator adjustment programs. See, e.g., 84 Fed. Reg. 17,454, 17,460 (April 25, 2019) ("We are not making changes to further implement the enrollee cost-sharing transparency requirements under § 156.220(d) as part of this rule.").

[39] 85 Fed. Reg. 37,286, 37,298 (June 19, 2020).

[40] Choice Plan Health Plan, Inc. v. Azar, 315 F. Supp. 3d 440, 443 (D.D.C. 2018).

[41] Int'l Union, United Mine Workers of Am. v. Mine Safety & Health Admin., 626 F.3d 84, 93 (D.C. Cir. 2010).

[42] Az. Cattle Growers' Ass'n v. Salazar, 606 F.3d 1160, 1163 (9th Cir. 2010).

Moreover, contrary to CMS' unsupported assumptions, an assessment of the CMS proposal by an outside analyst concludes that: "While manufacturers can establish program eligibility criteria, there is not currently a reliable method by which manufacturers can ensure in all cases that the assistance they offer is applied exclusively to the benefit of the patient. Determination of how the value of manufacturer assistance funds is accounted for is made solely by the health plan sponsor."[43] And CMS may not "ignore evidence contradicting its position"[44] or offer only "[c]onclusory explanations for matters involving a central factual dispute where there is considerable evidence in conflict."[45] Rather, CMS is required to "reasonably reflect upon the information contained in the record and grapple with contrary evidence."[46] Beyond "conclusory statements" that are not even comprehensible, CMS has offered nothing to support the assumptions that underlie this rulemaking. Nor has CMS addressed evidence that is contrary to these assumptions. Thus, CMS' analysis, based upon assumptions that "lack[] support in the record," is arbitrary and capricious.[47]

Finally, the proposed rule fails to consider the far-reaching impacts that the proposed changes could have on government price reporting and programs like Medicare and the 340B drug discount program. The proposed rule would also require that a manufacturer "ensure" that a plan has not applied an accumulator adjustment program to exclude patient assistance from AMP, which affects the 340B ceiling price (which equals AMP minus the Medicaid unit rebate amount, and would be affected by changes in AMP and best price[48]) and could drive down the Medicare Part B average sales price (ASP) and otherwise reduce Part B drug payments. Many manufacturers exclude from their calculation of ASP prices exempt from inclusion in best price, including patient assistance, and thus may include patient assistance in ASP if it is included in best price. Further, the ASP statute and regulations require that 103 percent of AMP be substituted for the ordinary Part B payment rate (106 percent of ASP) if the ASP for a drug exceeds AMP by 5 percent or more for two consecutive quarters,[49] meaning that a decline in AMP could cause such a substitution and thus reduce the Part B drug payment rate. Reducing a drug's Part B payment rate (either through a decline in ASP or through a substitution of 103 percent of AMP) could have detrimental effects on Medicare Part B providers and could hinder patient access to critical drugs.[50]

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[43] Rich Fry, Co-Pay Programs: The CMS Best Price Revision, TrialCard (June 30, 2020), available at https://corp.trialcard.com/co-pay-programs-the-cms-best-price-revision/.

[44] Genuine Parts Co. v. EPA, 890 F.3d 304, 312 (D.C. Cir. 2018).

[45] Id.

[46] Fred Meyer Stores, Inc. v. Nat'l Labor Relations Bd., 865 F.3d 630, 638 (D.C. Cir. 2017).

[47] See Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto Ins., 463 U.S. 29, 43 (1983) (agency acts arbitrarily and capriciously if it entirely fails to "consider an important aspect of the problem"); WildEarth Guardians v. U.S. Bureau of Land Mgmt., 870 F.3d 1222, 1235 (10th Cir. 2017).

[48] 42 U.S.C. § 256b(a).

[49] 42 U.S.C. § 1395w-3a(d); 42 C.F.R. § 414.904(d)(3).

[50] See, e.g., Robert A. Dowling, Buy and Bill: Know the Nuances, Save Your Margins, Urology Times (Mar. 1, 2016), available at https://www.urologytimes.com/view/buy-and-bill-know-nuances-save-your-margins; Gregory

When promulgating rules affecting AMP and best price in the past, CMS has considered the impact of these rules on the 340B ceiling price and the Medicare Part B payment rate.[51] Here, CMS has not considered any of these potential impacts. Thus, failure to consider these potential impacts now could make this rulemaking "susceptible to claims that the rules were arbitrary and capricious for failing to consider an important aspect of the problem."[52] Further, If CMS finalizes this proposal, to the extent that CMS raises questions about whether manufacturers meet the regulatory standard by passing the full value of the assistance onto the consumer, CMS may cause manufacturers to pull back on patient assistance programs and thus cause patients to pay more in out-of-pocket costs: yet another important issue CMS has failed to consider in the proposed rule.

PhRMA urges CMS to recognize that it lacks statutory authority to finalize this ill-advised proposal and not to finalize the proposal.

B. Line Extensions

CMS proposes to define "line extension" as a "new formulation" (except abuse-deterrent formulations) and to define "new formulation" as "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,"[53] including but not limited to: "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."[54]

Accordingly, if adopted, the proposed rule could subject all of these categories of innovative drugs to higher Medicaid rebates calculated under the alternative rebate formula for line extensions, creating a high risk of discouraging innovation and depriving patients of revolutionary, potentially life-saving drugs. CMS never even considers these

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Twachtman, Proposal to Change Part B Drug WAC-Based Reimbursement Draws Criticism, Rheumatology News (Sept. 25, 2018), available at https://www.mdedge.com/rheumatology/article/175584/business-medicine/proposal-change-part-b-drug-wac-based-reimbursement.

[51] See, e.g., 81 Fed. Reg. 5,170, 5,213 (Feb. 1, 2016) (noting that concerns raised by commenters regarding "AMP being substituted for ASP" and "the potential impact of the buildup approach on ceiling prices set under the 340B program" were no longer relevant.).

[52] See Little Sisters of the Poor Saints Peter & Paul Home v. Pennsylvania, Nos. 19-431 & 19-545, 2020 WL 3808424, *12, *12 n. 12 (July 8, 2020) (noting that the Departments of Treasury, Labor, and Health and Human Services had "consistently taken the position that their rules had to account for RFRA in response to comments that the rules would violate that statute").

[53] 85 Fed. Reg. 37,286, 37,319 (June 19, 2020).

[54] Id.

risks in the proposed rule (as it must, to explain the proposal adequately[55]), which clearly contravenes the language and intent of the line extension provision. The statute expressly delineates the bounds of a "line extension": product alterations similar to changing an immediate release drug to an extended release formulation.[56] Congress passed this narrow definition to target "slight" changes in drugs, such as changes in color—the only example cited in the legislative history other than extended release drugs—and thus to avoid hampering pharmaceutical innovation. However, CMS' proposal, if finalized, would go well beyond the statutory text and purpose and instead discourage development of important product innovations critical to meeting patient needs.[57]

As companies work aggressively to advance biopharmaceutical treatments and meet new health threats during the COVID-19 public health emergency, it is essential for CMS to implement the Affordable Care Act's (ACA's) line extension provision in a way that adheres to the statute's text and maintains biopharmaceutical innovation. Below we discuss in detail the dangerous implications of CMS' proposal and the clear legal barriers to adoption of this legally impermissible proposal, which should not be finalized. [58]

1. The Proposed Rule's "Line Extension" Definition Could Curb Innovation and Restrict Patient Access to Life-Altering Medicines

a. The Proposed Rule Fails to Appreciate the Value of Innovative Combination Drugs in Patient Care

While combination drugs can revolutionize treatment options for patients, achieving such breakthroughs can pose substantial technological and practical challenges. Developing combination drugs is not as simple as combining several pre-existing drugs. A key concern is developing a tablet that keeps the various active ingredients from interacting negatively and that is not too large to swallow.[59] Developing a combination drug that meets these criteria is a resource-intensive process, requiring countless hours of research and development and clinical testing. CMS' sweeping proposal neglects to take into account the immense value and major technical challenges associated with developing combination drugs, threatening to deprive many vulnerable patient populations of future life-altering drugs.

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[55] See Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto Ins., 463 U.S. 29, 43 (1983) ("the agency must examine the relevant data and articulate a satisfactory explanation for its action including a rational connection between the facts found and the choice made.") (internal quotation omitted).

[56] Social Security Act (SSA) § 1927(c)(2)(C).

[57] Indeed, the proposed definition undermines Congress' establishment of a lower 17.1 percent minimum base rebate, which is intended to incentivize pediatric drug development and blood clotting factors. The proposed rule fails to acknowledge this conflict or to reconcile the inconsistency caused by CMS' proposal.

[58] We note that if CMS did finalize any proposal to define line extension and related terms the definitions could not be applied retroactively. See Bowen v. Georgetown Univ. Hosp., 488 U.S. 204, 204 (1988) ("grants of rulemaking authority will not be understood to encompass the power to promulgate retroactive rules unless that power is conveyed by express terms").

[59] Nazaneen Pourkavoos, Unique Risks, Benefits, and Challenges of Developing Drug-Drug Combination Products in a Pharmaceutical Industrial Setting, 2 Combination Products in Therapy 2 (2012).

For example, for patients infected with human immunodeficiency virus (HIV), combination, cocktail therapy in the form of once-daily, single-tablet, multi-class treatment regimens have become an integral part of disease management over the past decade. Previously, the standard of care was a multi-tablet regimen. Today, once-daily fixed-dose combinations are not only better tolerated but, by combining as many as four different therapies in a single tablet, dramatically reduce pill burden for patients and have been shown to be more likely to achieve the adherence levels necessary to prevent the development of viral resistance.

To take one example, Atripla—the first fixed-dose combination pill that combined different classes of already-approved antiretrovirals for treatment of HIV—would be included in CMS' proposed definition of line extensions. However, this revolutionary product provides the advantage of being a one-pill, once-a-day treatment for a condition that once required patients to take dozens of pills each day, thus improving patients' ability to adhere to their treatment and control HIV. Improved adherence is particularly crucial in HIV treatment, as it reduces the potential for viral resistance and helps to maintain low viral loads.

Like HIV patients, individuals suffering from chronic obstructive pulmonary disease (COPD) greatly benefit from combination drugs. Fixed-dose combinations allow a bronchodilator—to relax the muscles around the airway—and a corticosteroid—to reduce airway inflammation—to be delivered in the same inhalation device.[60] The convenience of taking one treatment for COPD is likely to improve adherence while also ensuring that patients receive both therapeutic agents.[61] Moreover, evidence shows that combination therapy with two drugs improves lung function and patient-reported outcomes more than using either of the two drugs alone.[62]

Patients benefit from drug combination products—relying on their therapeutic improvements over single ingredient drugs in many additional ways—including eliminating or minimizing side effects of the individual drugs while maintaining therapeutic efficacy; preventing the generation of drug-resistant viruses or bacteria in the treatment of infectious diseases; and producing synergies in efficacy far exceeding the summed effectiveness of the components administered alone.[63] For example, a fixed-dose combination provides significant clinical differences over individual components, via distinct mechanisms of action. By increasing patient adherence, they may improve clinical outcomes and prevent drug-resistant diseases[64] as well as reduce use of other medicines or health care services. For example, among

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[60] Hobart Lee et al., Treatment of Stable Chronic Obstructive Pulmonary Disease: the GOLD Guidelines, 88 Am. Family Physician. 655 (2013).

[61] Nicholas Gross, Combination Therapies for COPD (2015); available at http://www.medscape.com/viewarticle/843727.

[62] Eric Bateman, et al., Recent advances in COPD disease management with fixed-dose long-acting combination therapies, 8 Expert Rev. Respir. Med. 357 (2014).

[63] Sameer Saini, et al., Effect of medication dosing frequency on adherence in chronic disease, 15 Am. J. of Managed Care e22 (2009).

[64] See, e.g., Sripal Bangalore, et al., Fixed-dose combinations improve medication compliance: a meta-analysis, 120 Am. J. of Med. 713, 713, 716, 718 (2007).

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 adherence could produce $8 billion in savings annually.[65]

Moreover, the ACA's line extension provision explicitly precludes a combination product from being classified as a line extension. The statute provides: "the term 'line extension' means, with respect to a drug, a new formulation of the drug."[66] Congress' use of the singular articles "a" and "the" specify that a line extension must be derived from a single "parent" drug. However, combination drugs stem from two or more distinct parent drugs. In fact, the ACA's alternative rebate provision cannot even be applied to combination products. The statutory language turns on the additional rebate and AMP for "the original single source drug or innovator multiple source drug"[67] —but, as mentioned above, combination products have two or more parent drugs. Therefore, even if it were otherwise appropriate to classify combination products as line extensions (which it is not), this classification would be infeasible to implement as the alternative rebate formula would not work.

b. The Proposed Rule Could Jeopardize Important New Indications That Address Unmet Patient Needs

CMS proposes to classify new indications as line extensions if "marketed as a separately identifiable drug product." As discussed below, what constitutes a "separately identifiable drug product" is ill-defined. The only example CMS cites is a product sold under a new NDC. While PhRMA is not suggesting that the examples of new indications we provide below would constitute "separately identifiable drug products," we are concerned that CMS' proposal may classify them as such, disincentivizing manufacturers from undertaking the necessary research to pursue such indications. PhRMA believes that new indications, whether sold as the same or separately identifiable drug product, should be categorically excluded from the concept of line extensions. Any other approach fails to appreciate the public health importance of new indications, which improve the therapeutic options available to patients, including patient populations for whom no drugs have been FDA-approved. FDA's Center for Drug Evaluation and Research (CDER) noted in its 2019 report on new drug therapy approvals that (as in previous years) "many important advances in drug therapy approved in 2019 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."[68] This is illustrated in the examples below relating to treatments (and potential treatments) for cancer, Multiple Sclerosis, heart failure, and COVID-19.

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[65] Mark Roebuck et al., Impact of Medication Adherence on Health Services Utilization in Medicaid. 56 Med. Care 266 (2018).

[66] SSA § 1927(c)(2)(C) (emphasis added).

[67] SSA § 1927(c)(2)(C)(iii)(II) (emphasis added).

[68] CDER, New Drug Therapy Approvals 2019 (Jan. 2020); available at https://www.fda.gov/media/134493/download.

Cancer: The underlying nature of cancer—characterized by rapidly dividing, mutating, and traveling cells—can make drug development particularly challenging in oncology. Once, older chemotherapies would wipe out both cancerous and healthy cells, leading to many side effects. Fortunately, cancer drug development has progressed tremendously, including targeted therapies that can reduce unwanted side effects—based on the premise that a common mechanism of action can be deployed across disparate diseases. As an example, kinase inhibitors, which are typically small molecule oral dosage forms, represent a class of drugs that target a single mechanism that is associated with different types of cancer.[69] These additional cancer indications may not be identified until post-approval, and at great expense.

Multiple Sclerosis (MS): In 2018, a disease-modifying oral medication first approved in 2010 to treat adults with relapsing MS was approved to treat children age 10 years and older, becoming the first FDA-approved drug to treat MS in pediatric patients.[70] While patients generally experience onset of MS in adulthood, research suggests up to five percent of all people with MS have symptom onset before age 18.[71] As this example illustrates, developing new indications for pre-existing drugs can enhance treatment options for additional patient populations.

Heart Failure: Entresto—a combination drug originally approved in 2015 as a First-in-Class drug to reduce the risk of cardiovascular death and heart failure hospitalization in adults with chronic heart failure—received FDA approval in 2019 to treat symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients one year and older.[72,73] This pediatric indication was approved based on an analysis at 12 weeks from the 52-week PANORAMA-HF trial (which is currently ongoing at 129 clinical site in approximately 39 countries[74]) and represents a significant medical breakthrough for pediatric patients who would otherwise face a poor prognosis. Specifically, almost half of children diagnosed with systolic heart failure require a heart transplant before age five, and nearly one-third require a heart transplant or die within one year.[75]

COVID-19: Finally, nearly 800 clinical trials are underway in response to the COVID-19 crisis to investigate new uses for existing products, including antiviral and anti-inflammatory

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[69] Khushwant S. Bhullar et al., Kinase-targeted cancer therapies: progress, challenges and future directions, 17 Molecular Cancer 1 (2018).

[70] FDA, Center for Drug Evaluation and Research, Advancing Health through Innovation. 2018 New Drug Approvals, at 25 (Jan. 1, 2019); available at https://www.fda.gov/media/120357/download.

[71] National Multiple Sclerosis Society, Pediatric MS, https://www.nationalmssociety.org/What-is-MS/Who-Gets-MS/Pediatric-MS.

[72] FDA, Novel Drugs Summary 2015 (Jan. 12, 2016), https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/novel-drugs-summary-2015.

[73] Novartis, Novartis Entresto receives FDA approval for pediatric heart failure, helping to address critical unmet need for treatment options (Oct. 1, 2019). https://www.novartis.us/news/media-releases/novartis-entresto-receives-fda-approval-pediatric-heart-failure-helping-address.

[74] Id.

[75] Id.

medications currently used to treat cancer and other diseases.[76,77,78] Examples include a JAK inhibitor, currently FDA approved for three indications, that is being evaluated in Phase 3 clinical trials for severe COVID-19 complications, including cytokine storm and acute respiratory distress syndrome[79,80,81] and a kinase inhibitor currently FDA approved for two indications that is the subject of a Phase 2 clinical trial designed to investigate its safety and efficacy in hospitalized patients with COVID-19.[82,83]

Classifying new indications as line extensions, even if limited to "separately identifiable drug products," as CMS proposes, could chill innovative efforts in the midst of a global pandemic—a time when pharmaceutical advances to keep people safe are of paramount importance. Because establishing existing therapies' safety and efficacy for new indications requires a significant investment of resources, penalizing pharmaceutical manufacturers with higher rebates for undertaking these efforts is a dangerous and counterproductive policy that could halt future innovations like those described above.

c. The Proposed Rule Fails to Consider the Benefits of New Routes of Administration

The same concern applies to other products changes that are beneficial for patients, such as developing and obtaining FDA approval for a new route of administration for a drug product. A new route of administration for a drug expands patient choice and may allow a patient to select an option that could improve tolerability or the overall clinical outcome. For example, long-acting injectables (LAIs) have emerged as a new treatment option for patients with schizophrenia, enabling patients to receive an injection administered by a health care

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[76] PhRMA, PhRMA COVID-19 Treatment Progress (last updated July 13, 2020), available at https://phrma.org/Coronavirus/Activity-Tracker.

[77] Seif Farhad, et al., JAK Inhibition as a New Treatment Strategy for Patients with COVID-19, 181 Int'l Archives of Allergy and Immun. 467 (2020).

[78] Mark Roschewski, et al., Inhibition of Bruton tyrosine kinase in patients with severe COVID-19, 5 Science Immun. (2020).

[79] JAKAFI Prescribing Information, available at https://www.jakafi.com/pdf/prescribing-information.pdf.

[80] U.S. National Library of Medicine, Phase 3 Randomized, Double-blind, Placebo-controlled Multi-center Study to Assess the Efficacy and Safety of Ruxolitinib in Patients With COVID-19 Associated Cytokine Storm (RUXCOVID) (last updated July 14, 2020), available at https://www.clinicaltrials.gov/ct2/show/NCT04362137.

[81] U.S. National Library of Medicine, A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Assess the Efficacy and Safety of Ruxolitinib in Participants With COVID-19-Associated ARDS Who Require Mechanical Ventilation (RUXCOVID-DEVENT) (last updated June 16, 2020), available at https://clinicaltrials.gov/ct2/show/NCT04377620.

[82] CALQUENCE Prescribing Information, available at https://www.azpicentral.com/calquence/calquence.pdf#page=1.

[83] U.S. National Library of Medicine, Acalabrutinib Study With Best Supportive Care Versus Best Supportive Care in Subjects Hospitalized with COVID-19. (CALAVI) (last updated May 11, 2020), available at https://clinicaltrials.gov/ct2/show/NCT04346199.

professional every few weeks or months. The key feature of LAIs is their ability to reduce the variability in self-administered dosing and help maintain more consistent levels of medicine over sustained periods of time. By allowing for a slower, steady release of medicine, LAIs can help manage symptoms of psychosis and lower the chances of relapse and hospitalizations. LAIs have also been shown to have a role in improving adherence and reducing resource utilization costs in Medicaid programs. For example, among Medicaid beneficiaries with schizophrenia, improving adherence to antipsychotic medicines generated annual net savings of up to $3.3 billion, or $1,580 per patient per year, driven by lower hospitalizations, outpatient care, and criminal justice system involvement.[84,85] Nevertheless, such a change would apparently constitute a "line extension" subject to the alternative URA calculation.

2. The CMS Proposal Conflicts with—and Undercuts—FDA Policies Encouraging the Approval of New Therapeutic Options for Patients

The proposed rule's definition of "line extension" would undermine a number of FDA policies and statutory provisions adopted to promote the public health and address unmet patient needs and may discourage manufacturers from undertaking the very research and development efforts that Congress and FDA have sought to incentivize. Such an outcome would be detrimental to patients. This section outlines several examples of conflicts between the proposed rule and FDA policies, involving: combination drugs, new indications, and new strengths.

a. CMS' Proposal Undercuts FDA's Affirmative Policy to Encourage Development of Combination Drugs

CMS recognizes that new combination drugs—such as products that "contain[] a new molecular entity in combination with a previously approved combination drug"—" —can be "very different from the initial brand name listed drug."[86] Nevertheless, CMS "believe[s] that [a new combination drug] is a new formulation of an initial brand name listed drug,"[87] which would constitute a line extension subject to the alternative URA calculation under the proposed rule. The only limiting principles under the proposed rule are that the new combination drug must share at least one active ingredient with an initial brand name listed drug and both products must have the same manufacturer (or there is a corporate relationship between the manufacturers).

This position conflicts with and undermines FDA's carefully considered policies intended to encourage the development of combination drugs. As FDA has explained in guidance, "fixed-combinations have become increasingly prevalent in certain therapeutic areas (including cancer, cardiovascular, and infectious disease) and … play an important role in optimizing adherence to

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[84] Zachary S. Predmore, et al., Improving Antipsychotic Adherence Among Patients With Schizophrenia: Savings for States, 66 Psychiatric Services in Advance 343 (2015).

[85] Rimal Bera, et al., Hospitalization Resource Utilization and Costs Among Medicaid Insured Patients With Schizophrenia With Different Treatment Durations of Long-Acting Injectable Antipsychotic Therapy, 34 J. of Clinical Psychopharmacology 30 (2014).

[86] 85 Fed. Reg. 37,286, 37,295 (June 19, 2020).

[87] Id.

dosing regimens and improving patient outcomes."[88] FDA thus "has adopted policies aimed at encouraging the development of fixed-combinations because, among other things, such combinations have been shown to improve treatment response, lower the risk of developing resistance, and lower the rates of adverse events."[89]

For example, FDA revised its historical interpretation of the provisions governing a combination drug's eligibility for new chemical entity (NCE) exclusivity. FDA's historical interpretation deemed a combination drug ineligible for 5-year NCE exclusivity if it contained any previously approved active moiety, even if it also contained a new active moiety.[90]

Under the revised policy, a combination drug would be eligible for 5-year NCE exclusivity if it "contains" a new active moiety.[91] FDA issued this revised interpretation with the express purposes of "further incentiviz[ing] the development of certain fixed-combination products"[92] and "align[ing] the exclusivity incentives more closely with [the agency's] public health goals."[93] In doing so, FDA acknowledged that its historical interpretation "may result in drug development strategies that are suboptimal from a public health perspective."[94] Indeed, FDA's guidance specifically highlighted one example of the revised interpretation: "a fixed-combination drug product that contains a drug substance with a single, new active moiety would be eligible for 5-year NCE exclusivity, even if the fixed-combination also contained a drug substance with a previously approved active moiety."[95]

CMS' proposed rule conflicts with FDA policy, noting "if a new combination drug contains a new molecular entity in combination with a previously approved drug, the resultant new combination may appear to be very different from the initial brand name listed drug, however, we believe that it is a new formulation of an initial brand name listed drug."[96] One example of such a combination product—in which new molecular entities are combined with previously approved drugs—is Stribild. Approved by the FDA in 2012 as a single-tablet treatment for HIV, Stribild consists of two previously approved medicines (emtricitabine and tenofovir disoproxil fumarate) combined with two novel medicines (elvitegravir and cobicistat).

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[88] FDA, Guidance for Industry: New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products (Oct. 2014), at 1.

[89] Id. at 7.

[90] FDA, Consolidated Response to Docket Nos. FDA-2013-P-0058, FDA-2013-P-0019, and FDA-2013-P-0471 (Feb. 21, 2014) (FDA Consolidated Response), at 11.

[91] FDA, Guidance for Industry: New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products (Oct. 2014), at 8.

[92] Id. at 1.

[93] Id. at 8.

[94] FDA, Consolidated Response to Docket Nos. FDA-2013-P-0058, FDA-2013-P-0019, and FDA-2013-P-0471 (Feb. 21, 2014), at 15.

[95] FDA, Guidance for Industry: New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products (Oct. 2014), at 8 (emphasis added).

[96] 85 Fed. Reg. 37,286, 37,295 (June 19, 2020) (emphasis added).

The addition of these two new molecular entities have dramatically improved both the tolerability of the new product and patient adherence, compared to earlier antivirals so that, by 2015, Stribild was recommended as an initial treatment for HIV in HHS guidelines while an earlier combination was not.[97] Such a groundbreaking product goes far beyond the "slight alterations" Congress targeted in enacting the line extension provision. Because of continued investment in research and development, today there are 18 combination tablets approved to treat HIV, revolutionizing the treatment paradigm for patients with previously complex treatment regimes.[98]

By classifying combination drugs as line extensions, the CMS proposed rule, if finalized, would undercut FDA's policy to encourage development of combination drugs and the broader public health objective of incentivizing the development of such products. The proposed rule arguably would encourage the "suboptimal drug development strategies" that FDA sought to address when adopting its revised interpretation of the NCE exclusivity statutory provisions, such as developing two drugs as separate, cross-labeled products rather than in a fixed combination.[99] In fact, the proposed rule specifically applies its approach to the very combination drugs for which FDA revised its historic approach to exclusivity to specifically encourage for public health purposes: new combination drugs containing a new molecular entity and a previously approved drug.[100] This conflict illustrates one key example of the ways in which the proposed rule could jeopardize pharmaceutical innovations critical to improving patient care.

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[97] Ed L. Wilkins et al., Patient-reported outcomes in the single-tablet regimen (STaR) trial of rilpivirine/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate in antiretroviral treatment-naive ddults infected with HIV-1 through 48 weeks of treatment, 28 AIDS Care 401 (2016).

[98] Jean B. Nachega, et al., Lower Pill Burden and Once-Daily Antiretroviral Treatment Regimens for HIV Infection: A Meta-Analysis of Randomized Controlled Trials, 58 Clin. Infectious Dis. 1297 (2014). See also U.S. Department of Health and Human Services, AIDS Info, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV, at 213 (Oct. 25, 2018), available at https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf (citing regimen simplification as achieving higher levels of adherence); Sally L. Hodder, et al., Patient-reported outcomes in virologically suppressed, HIV-1-infected subjects after switching to a simplified, single-tablet regimen of efavirenz, emtricitabine, and tenofovir DF, 24 AIDS Patient Care STDS 87 (2010), available at http://www.ncbi.nlm.nih.gov/pubmed/20156091; Calvin J. Cohen, et al., Association between daily antiretroviral pill burden and treatment adherence, hospitalisation risk, and other healthcare utilisation and costs in a US Medicaid population with HIV, 3 BJM Open 8 (2013), available at http://www.ncbi.nlm.nih.gov/pubmed/23906955; William R. Truong, et al., Once-Daily, Single-Tablet Regimens For the Treatment of HIV-1 Infection, 40 Pharm. & Therapeutics 44 (2015), available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4296592.

[99] See FDA, Consolidated Response to Docket Nos. FDA-2013-P-0058, FDA-2013-P-0019, and FDA-2013-P-0471 (Feb. 21, 2014) (FDA Consolidated Response), at 16.

[100] 85 Fed. Reg. 37,286, 37,295 (June 19, 2020).

b. CMS' Proposal Undercuts FDA Policy and Statutory Incentives Encouraging New Indications

CMS also has proposed that a new indication for a previously approved drug would be a line extension, if the manufacturer "markets the drug in such a way that it is a separately identifiable drug product."[101] It is unclear, however, what constitutes a "separately identifiable drug product," other than use of a new NDC. As discussed below, new indications are uses of a drug and are distinct from the drug's formulation.

Furthermore, this limitation is ill-defined and draws an arbitrary distinction without mitigating concerns that the proposal would penalize manufacturers for seeking and obtaining FDA approval of new indications. This approach fundamentally misconstrues the public health importance of obtaining FDA approval of secondary indications and would undermine statutory incentives encouraging the development of new uses for previously approved products.

The COVID-19 public health emergency illustrates the importance and public health benefit of identifying and studying new uses for an approved drug. FDA "continues to work with partners across the U.S. government and regulated industry to expedite the development and availability of critical medical products to prevent and treat this novel virus, including repurposing existing therapies that may help treat patients with COVID-19."[102] Indeed, in June 2020, FDA and the Critical Path Institute initiated a public-private partnership to pursue this objective, among others.[103] The proposed rule nevertheless would apply a penalty if a new COVID-19 indication is marketed as "a separately identifiable drug product," thus discouraging the very innovation that FDA hopes to foster to combat this public health emergency.

The proposed rule also would undermine longstanding statutory incentives that encourage the development and approval of new indications, among other types of innovation—*e.g.*, 3-year exclusivity for new clinical investigations, orphan-drug exclusivity, and pediatric exclusivity. We acknowledge that Congress identified extended-release formulations (which could be eligible to receive 3-year exclusivity in certain cases) as an example of line extensions. The proposed rule's broad interpretation of a "line extension," however, reaches far beyond extended-release formulations and diminishes the incentives that Congress intended to create.[104] As discussed below in section B.3.a, Congress meant for the term "line extension" to cover only a limited set

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[101] 85 Fed. Reg. 37,286, 37,296 (June 19, 2020).

[102] FDA News Release, Coronavirus (COVID-19) Update: FDA Continues to Facilitate Development of Treatments (Mar. 19, 2020), available at https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-continues-facilitate-development-treatments (emphasis added).

[103] See Critical Path Institute, CURE Drug Repurposing Collaboratory, available at https://c-path.org/programs/cdrc/ (identifying one of CRDC's objectives as "[e]valuat[ing] drug leads through advanced analytics to identify candidates for repurposing as new treatments in a transparent open forum").

[104] A product change should not constitute a line extension if it requires clinical studies of safety and effectiveness (i.e., not bioavailability or bioequivalence studies) for FDA approval. Congress established statutory incentives to encourage the continued study and development of drugs after their initial FDA approval. These studies support further innovation, such as the discovery of a new use for an approved drug, that can offer meaningful public health benefits by expanding the therapeutic options available to patients (including patient populations who may not otherwise have an FDA-approved treatment for a disease or condition).

of drugs that represented "slight alternations" in an existing drug. Classifying new indications as line extensions would undermine crucial statutory incentives that otherwise could help us fight the COVID-19 crisis: a dangerous use of the line extension provision that goes far beyond what Congress authorized.

Finally, the proposed rule classifies a labeling change (*i.e.*, for a new indication) as a formulation change even where there has been no change to the product itself. This proposal conflicts with the Federal Food, Drug, and Cosmetic Act (FDCA) and the FDA regulatory concept of a "formulation." FDA does not consider a drug's labeling to be a component of that product's "formulation."[105] The FDCA and FDA's regulations for generic applications illustrate this distinction. For example, FDA generally permits generic drugs to differ from the reference listed drug in formulation but cannot approve a new indication for generic drugs if the indication has not been approved for the reference listed drug.[106]

Defining a "new formulation" to include new indications (or other changes submitted to FDA) when the product itself is exactly the same would contradict the widely accepted understanding of terminology falling within FDA's scientific expertise and jurisdiction, and undermine the purpose of the regulatory exclusivity periods administered by the agency. A new indication for an approved drug should not be considered a line extension, regardless of how the manufacturer chooses to market the product.

c. CMS' Proposal Fails to Appreciate the Importance of New Strengths

CMS proposes to identify "a new strength of a drug, produced or distributed at a later time than the initial strength(s)" as a line extension subject to the alternative URA calculation.[107] According to the proposed rule, CMS "believe[s] a change in strength is a relatively simple modification to a currently marketed product."[108] Moreover, the preamble speculates that a manufacturer may "change the strength of a drug that is losing its exclusivity or patent protection to prolong the lifecycle of the drug, preventing money saving generic substitution."[109]

CMS' proposed approach suggests a fundamental misunderstanding of the patient needs that different strengths serve. The availability of multiple different strengths for a drug improves a patient's dosing options, which allow for more precise dosing tailored to a patient's needs. For example, this precision can allow patients to identify an appropriate dosing regimen that could improve tolerability and/or reduce adverse events. Multiple strengths also can boost patient adherence to the prescribed therapy and offer greater convenience for patients due to a reduced pill burden, which can improve patient outcomes. As an example, a patient may be more likely to

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[105] See FDA, Guidance for Industry: Determining Whether to Submit an ANDA or a 505(b)(2) Application (May 2019), at 8 (explaining that a generic application must include information regarding the identity and quantity of all active and inactive ingredients of the proposed drug product (i.e., the formulation) . . . .") (emphasis added).

[106] See 21 C.F.R. §§ 314.54 and 314.94.

[107] 85 Fed. Reg. 37,286, 37,296 (June 19, 2020).

[108] 85 Fed. Reg. 37,286, 37,295 (June 19, 2020).

[109] 85 Fed. Reg. 37,286, 37,296 (June 19, 2020).

comply with a long-term dosing regimen of taking one capsule of a drug each day, as opposed to multiple capsules every day. For example, Lynparza® (olaparib) was first approved with a recommended dose of 400 mg (eight 50 mg capsules) taken twice daily for a total daily dose of 800 mg.[110] FDA later approved Lynparza in a tablet dosage form with a recommended dose of 300 mg (two 150 mg tablets) taken twice daily for a total daily dose of 600 mg.[111] A 100 mg tablet is also available for dose reduction.[112]

These benefits of additional strengths are meaningful to patients, but the proposed rule would subject additional strengths of an approved drug to the alternative URA calculation, thus penalizing manufacturers for making these additional options available for patients.

In addition, CMS makes an unfounded generalization about why a manufacturer might obtain approval for different strengths of the same drug at different times. A manufacturer may seek approval of a new strength of a drug to meet patient demand and offer enhanced therapeutic options. Alternatively, a manufacturer may seek approval for multiple strengths in an original application, with FDA approving only a subset of those strengths. For example, FDA may require additional safety data to support the approval of a higher strength or, conversely, the agency may require the manufacturer to provide additional efficacy data for a lower strength. Under the proposed rule, if a manufacturer in this scenario submitted additional data to demonstrate that the strength presents a favorable benefit-risk profile, CMS would deem the strength approved later-in-time to be a line extension subject to the alternative URA calculation. Rather than encouraging manufacturers to take steps that would expand patients' treatment options, this approach would penalize manufacturers for investing in and pursuing additional improvements to a drug.

Furthermore, despite the proposed rule's suggestion that a new strength is a "simple modification," such a change must be supported by data—which may require conducting clinical trials—and receive FDA approval.

Finally, as with new indications, the proposed approach does not square with FDA's conception of a "formulation," which is commonly understood to refer to a drug product's active and inactive ingredients.[113] Generic drugs, for example, may vary from their reference listed drugs in "formulation" due to differences in inactive ingredients,[114] yet are statutorily required to have the same strength.[115] Defining "new formulation" to include a new strength conflicts with the FDCA and the FDA regulatory understanding of "formulation."

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[110] Lynparza Capsules Prescribing Information, Dosage and Administration: Recommended Dosing (Dec. 2014).

[111] Lynparza Tablets Prescribing Information: Dosage and Administration: Recommended Dosing (Aug. 2017).

[112] Id.

[113] See FDA, Guidance for Industry: Determining Whether to Submit an ANDA or a 505(b)(2) Application (May 2019), at 8.

[114] FDA, Guidance for Industry: Determining Whether to Submit an ANDA or a 505(b)(2) Application (May 2019), at 8.

[115] 21 U.S.C. § 355(j)(2) (FDCA § 505(j)(2)).

3. The CMS Exceeds its Statutory Authority and is Legally Impermissible

a. Legislative History

In addition to the dangerous practical implications of CMS' proposal, discussed above, the proposal exceeds the authority Congress granted to CMS in enacting the line extension provision. Specifically, the ACA defined a "line extension" as "a new formulation of the [oral solid dosage form innovator] drug, such as an extended release formulation," and the legislative history repeatedly described a line extension as a "slight alteration" of an existing drug.[116] Yet CMS now would define a line extension as a "new formulation" of an oral solid dosage form drug that represents "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, including, but not limited to: 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."[117]

This proposed definition goes far beyond the statutory language and Congress' intent to increase rebates only for "slight" alterations in a drug. The history leading up to the line extension provision shows that it resulted from concerns that drug manufacturers could make "slight" changes to an existing drug and (because the slightly different product would call for a new NDC and have a different base date AMP and additional rebate) pay a lower additional rebate for the slightly different product than the additional rebate for the "parent" drug. Since the start of this discussion, though, the proposals for change were aimed exclusively at what Congress considered to be "slight" changes in existing products.

HHS Office of Inspector General (OIG) work plans identified this issue for many years. For example, the OIG Work Plan for 2001 described a project to "analyze the effect of new versions of existing drugs on the Medicaid drug rebate program,"[118] explaining that:

> Part of the rebate calculation for brand name drugs is based on an inflation adjustment. The rebate is the amount by which the current average manufacturers' price for a drug exceeds the base average manufacturers' price, indexed to the consumer price index for urban consumers from the time a drug enters the market. Under current rules, a manufacturer could change a drug

[116] SSA § 1927(c)(2)(C) (emphasis added).

[117] 85 Fed. Reg. 37,286, 37,319 (proposed 42 C.F.R. § 447.502) (June 19, 2020).

[118] Department of Health and Human Services, Office of Inspector General, HHS/OIG Fiscal Year 2001 Work Plan, at 34.

> slightly (*e.g.*, a change in color) to obtain a new national drug code, resulting in a new start for indexing purposes.[119]

In December 2008, the Congressional Budget Office (CBO) released a budget options report repeating the same idea articulated by the OIG. Under current rebate rules, CBO reported, "drug makers can often avoid incurring an additional rebate obligation by making a slight alteration to an existing product."[120]

The legislative history of the ACA and the bills leading up to it repeatedly struck the same theme. A May 2009 Senate Finance Committee Options Paper stated that "drug makers can avoid incurring additional rebate obligations by making slight alterations to existing products, sometimes called line-extensions."[121] The Options Paper thus defined "line-extensions" as "slight alterations to existing products." It went on to explain: "This option would consider line-extensions of existing drugs as if they were the original product for purposes of calculating the additional rebate. Under this option, when a new, extended release version of an existing drug is introduced, the additional rebate obligation would be [based on then-applicable law or a new concept]."[122]

The Chairman's Mark concerning the Senate Finance Committee's health reform bill (the America's Healthy Future Act of 2009) again referred exclusively to extended release formulations, and again stated that manufacturers could "avoid incurring additional rebate obligations by making slight alterations to existing products."[123] The Senate Finance Committee's report on this bill again equated line extensions with "slight alterations" in existing products, stating that: "drug makers sometimes can avoid incurring additional rebate obligations by making slight alterations to existing products, sometimes called line-extensions."[124]

The House health reform bill leading up to the ACA (the America's Affordable Health Choices Act of 2009) increased rebates on line extensions and defined "line extension" exclusively as "an extended release formulation of the drug."[125] Likewise, a House

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[119] Department of Health and Human Services, Office of Inspector General, HHS/OIG Fiscal Year 2001 Work Plan, at 34-35 (emphasis added).

[120] CBO, Budget Options Volume I, Health Care (Dec. 2008) at 143 (emphasis added).

[121] Senate Finance Committee, Description of Policy Options, Financing Comprehensive Health Care Reform: Proposed Health Systems Savings and Revenue Options (May 20, 2009) at 12 (emphasis added).

[122] Id.

[123] Senate Committee on Finance Chairman's Mark, America's Healthy Future Act of 2009, at 54 (Sept. 2009) (emphasis added).

[124] Senate Finance Committee Rep. No. 111-89, at 92 (Sept. 2009) (emphasis added).

[125] America's Affordable Health Choices Act of 2009, H.R. 3200, 111th Congress, at 854-55 (2009).

Energy and Commerce Committee Report on this bill only identified extended release formulations as "line extensions."[126]

In short, the history of this provision consistently makes the same few points: (1) the line extension/new formulation provision was designed to address the concern that "slight" changes to existing products enabled manufacturers to reset base date AMP and thereby reduce their rebates; (2) "line extensions" were specifically described as "slight alterations to existing products"; and (3) the focus throughout was on extended release products. Thus, the legislative history equates line extensions with "slight" changes and contains zero evidence that Congress believed it might affect incentives for innovation; instead, all Congress had in mind was shutting down what it saw as a rebate "loophole." No risk to innovation was ever cited, because none was even envisioned.

While Congress seems to have considered extended release version of medicines as "slight" changes for purposes of this policy and includes them as line extensions in the statute, these medicines can have profoundly important clinical benefits over their precursors such as improving adherence to needed treatment.[127] Poor adherence is a major public health problem generating high avoidable clinical and economic costs; any mechanism that improves adherence is an important advance.[128]

b. The CMS Proposal is Inconsistent with the Statutory Language

CMS' proposed definition of a line extension would capture far more than Congress intended in the ACA's line extension provision. The only example of a line extension cited in the statute is extended release products. Under the ejusdem generis principle used in statutory interpretation, "where general words follow an enumeration of specific items, the general words are read as applying only to other items akin to those specifically enumerated."[129] Under this canon of construction, the only products that could potentially be classified as line extensions are those reflecting a slight alteration to an existing drug, "such as an extended release formulation."

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[126] H.R. Comm. on Energy and Commerce Rep. No. 111-299, at 635 (2009).

[127] David V. Sheehan et al., Differences in Medication Adherence and Healthcare Resource Utilization: Older Versus Newer Antidepressant Agents in Patients with Depression and/or Anxiety Disorders, 22 CNS Drugs 963 (2008); Christopher M. Dezii, et al., Effects of Once-Daily and Twice-Daily Dosing on Adherence With Prescribed Glipizide Oral Therapy for Type 2 Diabetes, 95 South Med. J. 68 (2002); Sameer D. Saini, et al., Effect of Medication Dosing Frequency on Adherence in Chronic Diseases, 15 Am. J. Manag. Care 22 (2009); Ami J. Claxton, et al., A Systematic Review of the Associations Between Dose Regimens and Medication Compliance, 23 Clin. Therapeutics 1296 (2001).

[128] Lars Osterberg & Terrence Blaschke, Adherence to Medication, 353 N. Engl. J. Med. 487 (2005); William H. Shrank et al., A blueprint for pharmacy benefit managers to increase value, 15 Am. J. Manag. Care 87 (2009).

[129] See, e.g., Harrison v. PPG Indus., Inc., 446 U.S. 578, 588 (1980); Circuit City Stores, Inc. v. Adams, 532 U.S. 105, 114-15 (2001); Washington Dep't of Social Servs. v. Keffeler, 537 U.S. 371, 384 (2003) (relying on both noscitur a sociis and ejusdem generis). Noscitur a sociis stands for the principle of that "words grouped in a list should be given related meaning." Dole v. United Steelworkers of Am., 494 U.S. 26, 36 (1990).

Accordingly, CMS must follow the ACA's language and confine line extensions (at most) to product alterations that do not go beyond those made by extended release formulations. CMS therefore must define "line extension" much more narrowly than it now proposes. The proposed rule ignores the statute's language and history and defines a line extension as nearly any product that stems in some way from an existing product and has at least one shared active ingredient. CMS fails to suggest any rationale for this troubling expansion of the line extension penalty; to consider how such an expanded penalty would affect biopharmaceutical innovation and patient care; or to consider whether its proposal aligns with the statute's only example of a line extension: extended release drugs.

Clearly CMS' proposed line extension definition is too broad to match Congress' goal of increasing rebates only on drugs it considered "slight" variations on existing products (such as extended release formulations). Any effort to expand the definition to a long list of product innovations that include "changes in dosage form, strength, route of administration, ingredients, pharmacodynamics, or pharmacokinetic properties; changes in indication . . . ; and combination drugs" plainly transcends the bounds Congress established. Given the long, consistent history of the ACA's line extension measure and the modest statutory text, an expansive definition of this category is not reasonable and not consistent with the ejusdem generis principle. CMS must be faithful to the text and legislative history and limit the line extension provision to the boundaries Congress expressly delineated.

c. The Statute Does Not Grant CMS the Unusually Broad Authority Claimed in CMS' Proposal

CMS has claimed far broader authority than Congress has granted to it in the statutory line extension provision, mentioning at least twice that the statute does not "expressly" preclude the broad definition it has proposed.[130] However, the courts have repeatedly rejected the theory that an agency has a certain authority because the statute in question did not expressly deny that power to the agency. The argument "that the disputed regulations are permissible because the statute does not expressly foreclose the construction advanced by the agency"—" —which is exactly the argument that CMS advances here—is "entirely untenable under well-established case law."[131]

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[130] See, e.g., 85 Fed. Reg. 37,286, 37,295 (June 19, 2020) ("The statutory definition of line extension does not expressly exclude combination drugs . . ."); id. ("The statutory definition of line extension does not expressly exclude a new strength of a drug . . .").

[131] Aid Ass'n for Lutherans v. USPS, 321 F.3d 1166, 1174 (D.C. Cir. 2003); see also, e.g., ExxonMobil Gas Mktg. Co. v. FERC, 297 F.3d 1071, 1088 (D.C. Cir. 2002) ("We have repeatedly admonished federal agencies that jurisdiction may not be presumed based solely on the fact that there is not an express withholding of jurisdiction."); Nat'l Mining Ass'n v. U.S. Dep't of Interior, 105 F.3d 691, 695 (D.C. Cir. 1997) (rejecting the "extreme position" that "because Congress did not specifically preclude" an agency action, the court "should defer to [the agency's] interpretation of the statute"); Am. Petroleum Inst. v. EPA, 52 F.3d 1113, 1120 (D.C. Cir. 1995) ("[W]e will not presume a delegation of power based solely on the fact that there is not an express withholding of such power."); Ethyl Corp. v. EPA, 51 F.3d 1053, 1060 (D.C. Cir. 1995) ("We refuse ... to presume a delegation of power merely because Congress has not expressly withheld such power.").

Where Congress has made a delegation of authority, agencies may not interpret the delegation in a manner that implicitly grants them powers beyond those envisioned by Congress.[132] CMS' proposed definition of line extension is far too broad to match Congress' goal of increasing rebates on drugs it considered "slight" variations on existing products (*e.g.*, extended release formulations). Stretching the line extension definition so far that it reaches (among other things) "changes in dosage form, strength, route of administration, ingredients, pharmacodynamics, or pharmacokinetic properties; changes in indication . . . ; and combination drugs" plainly exceeds the authority Congress granted CMS in the statute.[133] Agencies have discretion to fill gaps or interpret ambiguities in a statute in a reasonable manner, but their powers end there.

This principle has particular force where an agency claims that a statute "impliedly" empowers it to make important policy choices that Congress would be unlikely to delegate. The Supreme Court has held that decisions about whether a statute delegates certain powers to an agency "must be guided to a degree by common sense as to the manner in which Congress is likely to delegate a policy decision of . . . economic and political magnitude to an administrative agency"; Congress cannot be assumed to delegate such decisions to an agency in a "cryptic" fashion.[134] That is, congressional intent to delegate controversial policy decisions on key issues to an administrative agency cannot be inferred from Congressional silence or isolated cryptic phrases. As Justice Scalia explained in Whitman v. American Trucking Associations, Inc., Congress "does not alter the fundamental details of a regulatory scheme in vague terms or ancillary provisions—it does not, one might say, hide elephants in mouseholes."[135]

In applying this "elephant-in-mousehole" doctrine, courts have analyzed both the breadth of the powers claimed by an agency and the specificity of the delegation from Congress. Where the agency's interpretation would give it broad or unusual powers, courts are more likely to reject the agency's interpretation. For example, in FDA v. Brown & Williamson Tobacco Corp., the Supreme Court declined to defer to the FDA's view that it could regulate tobacco as a "drug" under the FDCA,[136]declaring that "we are confident that Congress could not have intended to

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[132] See, e.g., Adams Fruit Co. v. Barret, 494 U.S. 638, 650 (1990) (recognizing that "agency determinations within the scope of delegated authority are entitled to deference," but reiterating the "fundamental" principle "'that an agency may not bootstrap itself into an area in which it has no jurisdiction.'") (quoting Fed. Mar. Comm'n v. Seatrain Lines, Inc., 411 U.S. 726, 745 (1973)).

[133] Further, the statute only grants the Secretary express authority to determine whether a product is an abuse-deterrent formulation -- which is not to be treated as a line extension -- rather than authorizing the Secretary to determine whether a product is a line extension. In the line extension provision the parenthetical "as determined by the Secretary" is included in the clause that provides "but does not include an abuse-deterrent formulation," and is set off from the remainder of the sentence with commas. SSA § 1927(c)(2)(C) ("the term 'line extension' means, with respect to a drug, 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 . . .") (emphasis added). Under a natural read of this sentence the parenthetical only modifies the phrase "does not include an abuse-deterrent formulation of the drug."

[134] FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 160 (2000).

[135] Whitman v. Am. Trucking Ass'ns, Inc., 531 U.S. 457, 468 (2001).

[136] FDA v. Brown & Williamson Tobacco Corp., 529 U.S. 120, 160 (2000).

delegate a decision of such economic and political significance to an agency in so cryptic a fashion."[137] Similarly, in MCI Telecommunications Corp. v. American Telephone and Telegraph Co., the Court held that the Federal Communications Commission (FCC) did not have the authority to relieve certain carriers from statutory rate-filing requirements.[138] "Bearing in mind . . . the enormous importance to the statutory scheme of the tariff-filing provision," the Court reasoned that "[i]t is highly unlikely that Congress would leave the determination of whether an industry will be entirely, or even substantially, rate-regulated to agency discretion."[139] Likewise, in Gonzales v. Oregon, the Court cited Whitman and Brown & Williamson and held that "[t]he importance of the issue [in question], which has been the subject of an 'earnest and profound debate' across the country, makes the oblique form of claimed delegation all the more suspect."[140]

Courts are also more likely to reject an agency interpretation of general or vague statutory language. In Whitman, the Court held that a Clean Air Act provision did not authorize the Environmental Protection Agency (EPA) to consider economic costs by authorizing EPA to set air quality standards "requisite to protect the public health."[141] The Court held that it was "implausible that Congress would give to the EPA through these modest words the power to determine whether implementation costs should moderate national air quality standards."[142] The MCI Telecommunications Court also focused on the vague statutory language at issue, reasoning that the FCC's statutory authority to "modify" rate-filing requirements did not permit "basic and fundamental changes" to the statutory scheme.[143] The Court found it unlikely that Congress would leave decisions about whether an industry would be rate-regulated to agency discretion—and "even more unlikely that it would achieve that through such a subtle device as permission to 'modify' rate-filing requirements."[144]

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[137] Id.

[138] MCI Telecomms. Corp. v. Am. Tel. & Tel. Co., 512 U.S. 218, 234 (1994).

[139] MCI Telecomms. Corp. v. Am. Tel. & Tel. Co., 512 U.S. 218, 231 (1994).

[140] Gonzales v. Oregon, 546 U.S. 243, 267 (2006).

[141] Whitman v. Am. Trucking Ass'ns, Inc., 531 U.S. 457, 472 (2001) (quoting 42 U.S.C. § 7409(b)(1)).

[142] Whitman v. Am. Trucking Assn's, Inc., 531 U.S. 457, 468-69 (2001) (Considering costs "is both so indirectly related to public health and so full of potential for cancelling the conclusions drawn from direct health effects that it would surely have been expressly mentioned . . . had Congress meant it to be considered.").

[143] MCI Telecomms. Corp. v. Am. Tel. & Tel. Co., 512 U.S. 218, 225 (1994).

[144] MCI Telecomms. Corp. v. Am. Tel. & Tel. Co., 512 U.S. 218, 231 (1994); see also, e.g., Am. Library Assoc. v. FCC, 406 F.3d 689, 704 (D.C. Cir. 2005) ("We can find nothing in the statute, its legislative history, the applicable case law, or agency practice indicating that Congress meant to provide the sweeping authority the FCC now claims over receiver apparatus. . . . As the Supreme Court has reminded us, Congress 'does not ... hide elephants in mouseholes.'"); Bilski v. Kappos, 561 U.S. 593, 645 (2010) (Stevens, J., concurring) ("Particularly because petitioners' reading of the 1999 Act would expand § 101 to cover a category of processes that have not 'historically been eligible' for patents, we should be loathe to conclude that Congress effectively amended § 101 without saying so clearly."); In re Any and all Funds or Other Assets, In Brown Brothers Harriman & Co. v. Opportunity Fund and Tiger Eye Investments, Ltd., 613 F.3d 1122, 1129-30 (D.C. Cir. 2010) ("[U]nder the Government's interpretation, a U.S. citizen's assets could be frozen for years -- without any meaningful substantive judicial review in a U.S. court . . . . Here, as elsewhere, it is difficult to believe Congress would 'enact so significant a [measure] without a clear

(continued…)

A recent decision by the District of Columbia Circuit similarly rejected an agency effort to find sweeping powers in more limited statutory language. In Merck & Co. v. United States Department of Health and Human Services, the District Court for the District of Columbia struck down a CMS rule requiring drug manufacturers to disclose wholesale acquisition costs of 30-day supplies of drugs in television advertisements, holding that "the SSA's [Social Security Act's] absence of an express limitation does not enable HHS to arrogate to itself the power to regulate drug marketing as a means of improving the efficiency of public health insurance programs."[145] The Court of Appeals for the D.C. Circuit affirmed the district court's ruling on appeal, noting (among other things) that "the district court emphasized that the Disclosure Rule 'moves [the Department] into regulating the marketing of products that comprise 'a significant portion of the American economy[,]' and that Congress would not have authorized such sweeping and substantial regulatory power in a statutory provision that merely grants general administrative authority."[146]

The elephant-in-mousehole doctrine is particularly applicable here, where CMS' proposal would have a dangerous and widespread impact on the pharmaceutical industry and those who depend on it[147]—and the statute simply provides that a line extension is "a new formulation of the drug, such as an extended release formulation . . ."[148] Congress would not have implicitly authorized CMS, through such vague statutory language and without a single mention of this expansive authority in the statute's text or legislative history, to subject an expansive array of innovative and revolutionary drugs to higher rebates that could threaten innovation and the development of drugs critical to many patients. The statutory text and legislative history, discussed at length above, illustrate Congress' intent to impose the line extension rebate penalties on a narrow class of drugs that represent "slight" alterations of the parent drug, "such as an extended release formulation."

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indication of its purpose to do so.' Congress does not typically hide elephants in mouseholes, and the Government's assertion of authority in this case qualifies as such an elephant.") (internal citations omitted).

[145] Merck & Co. v. HHS, 385 F. Supp. 3d 81, 93 (D.D.C. 2019), aff'd, 962 F.3d 531, 2020 WL 3244013 (D.C. Cir. June 16, 2020).

[146] Merck & Co. v. HHS, 962 F.3d 531, 2020 WL 3244013, at *3 (D.C. Cir. June 16, 2020).

[147] Moreover, in formulating policies that have takings implications, agencies must (among other things) "be sensitive to, anticipate, and account for, the obligations imposed by the Just Compensation Clause of the Fifth Amendment … so that they do not result in the imposition of unanticipated or undue additional burdens on the public fisc." Executive Order 12630 Sec. 3(a). Here, finalizing the proposed line extension definition would raise serious concerns of a Fifth Amendment Taking, particularly as CMS would be diminishing the value of many drugs with exclusivity. See, e.g., Laurence Tribe, 147 Cong. Rec. E2286-88 (Nov. 13, 2001), Memorandum to the United States Congress--Constitutional Analysis of H.R. 2887's Proposed Amendment to Hatch-Waxman Act Eliminating Three-Year clinical Studies Exclusivity Period ("Under the Supreme Court's decision in Ruckelshaus v. Monsanto Co., 467 U.S. 986 (1984), and related precedent, the retroactive elimination of the exclusivity period qualifies as a taking of private property for public use and therefore triggers the right to just compensation").

[148] SSA § 1927(c)(2)(C) (emphasis added).

Accordingly, for all the reasons discussed above, CMS' proposed definition of line extension exceeds the powers granted to CMS by Congress and must not be adopted.[149]

C. Value-Based Arrangements

In the proposed rule, CMS sets forth a variety of changes to facilitate value-based arrangements. PhRMA appreciates these efforts and supports CMS' proposed changes to the "bundled sale" definition and to the period for restating Medicaid pricing information related to value-based arrangements (with certain clarifications). We also generally support the proposed definition of "VBP arrangement" and suggest some clarifying revisions to this definition. Finally, we request that CMS issue another, more detailed, proposed rule addressing the topic of multiple best prices.

For clarity, we refer to the concept of a "VBP arrangement" as a "value-based arrangement" or "VBA" throughout these comments, as they usually involve payors rather than purchasers. We believe the term "value-based arrangement" more accurately characterizes arrangements that may involve either payors or purchasers.

1. PhRMA Supports VBAs and Encourages CMS to Continue Efforts to Facilitate VBAs

PhRMA and its members strongly support CMS' efforts to facilitate VBAs. We believe that VBAs can improve patient care and optimize health care spending, ensuring that payments for drugs and biologics reflect the benefits they deliver to patients, the health system and society. We agree with past statements by HHS that VBAs can help improve health system sustainability and affordability by linking payment quality and value,[150] and we appreciate CMS' efforts to begin needed reforms in this proposed rule. VBAs can benefit patients and the health care system by improving health outcomes and other endpoints that matter, while reducing overall costs to payors and patients alike.

VBAs are voluntary arrangements that can include a wide range of contracts between manufacturers and payors, including arrangements that more explicitly link payment to a drug's real-world performance on clinical or patient health outcomes. VBAs can be used for a wide range of therapies, from treatments for chronic diseases like diabetes to breakthrough cell and gene therapies for rare diseases and conditions. Such arrangements hold drug manufacturers

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[149] Since CMS' proposal is precluded by the Medicaid statute CMS must not adopt its proposal but instead should allow manufacturers to continue to rely on reasonable assumptions in determining whether a drug qualifies as a line extension.

[150] See, e.g., CMS, Innovative Treatments Call for Innovative Payment Models and Arrangements (Aug. 30, 2017), available at https://www.cms.gov/newsroom/press-releases/cms-innovative-treatments-call-innovative-payment-models-and-arrangements ("[a]s part of larger efforts to support the President's priority [of lowering drug costs], CMS is working actively with all stakeholders . . . on innovative payment arrangements" including "outcome-based pricing for medicines . . . ."); 81 Fed. Reg. 5,169, 5,253 (Feb. 1, 2016) ("[W]e recognize the value of such [value-based] arrangements especially when they benefit patients.").

accountable for the results their products achieve, supporting patient health while channeling spending more effectively within the context of the VBA itself as well as in health care more broadly. Further, in shifting risk from payors to manufacturers (or allowing manufacturers and payors to share risk), VBAs can increase patient access to new medicines, including breakthrough therapies for rare and devastating diseases that previously lacked any effective treatment option. In the past, uncertainties about the degree to which a plan's member population would benefit from a breakthrough medicine may have discouraged payors from providing clinically optimal coverage for such treatments. VBAs also can enhance competition among manufacturers within a particular therapeutic area[151] and generate more information on the effects of different treatment regimens for different populations.[152] This increase in the evidence base, available for patients and physicians to make individualized treatment decisions, and for plans to structure coverage policies and formularies, can ultimately promote adoption of more effective therapies.

2. PhRMA Supports CMS' Proposed Changes to the "Bundled Sale" Definition

CMS proposes to amend the definition of "bundled sale" in 42 C.F.R. § 447.502 to clarify that a VBA may qualify as a bundled sale, "if the arrangement contains a performance requirement such as an outcome(s) measurement metric."[153] CMS explains that this approach "smooths out the discount over all the units sold under the arrangement," and notes that some manufacturers have already adopted reasonable assumptions recognizing VBAs as bundled sales pursuant to the existing regulatory text.[154] PhRMA supports CMS' proposal, which validates manufacturers' current practices and reasonable assumptions.

3. PhRMA Supports CMS' Proposed Flexibility for Pricing Restatements Involving VBAs

CMS proposes to amend current rules requiring manufacturers to revise Medicaid pricing data within 12 quarters (3 years) after the data was initially due. Under these rules, manufacturers may only restate pricing beyond this period in specified situations.[155] Because many arrangements involve outcomes- or evidence-based measures that extend beyond 3 years, or include installment payments outside a 3-year span, CMS proposes to allow manufacturers to make changes beyond the 3-year window in the case of VBAs that expand beyond this period.[156]

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[151] See, e.g., Lee Staley, A Drug's Worth: Why Federal Law Makes it Hard to Pay for Pharmaceutical Performance, 98 Boston Univ. Law Rev. 303 at 310 (2018) ("Tying reimbursement to health outcomes presents new opportunities for competition with rival manufacturers. . . . A manufacturer that can demonstrate sustained health benefits in post-market studies may distinguish itself from competitors.).

[152] For example, one study conducted in Sweden concluded that "stakeholders benefited from analysis of real-world (postmarket) data (in addition to pre-launch, trial-based data)" collected under a value-based pricing agreement. See Deloitte, Value-based Pricing for Pharmaceuticals: Implications of the Shift from Volume to Value (2012), available at http://deloitte.wsj.com/cfo/files/2012/09/ValueBasedPricingPharma.pdf.

[153] 85 Fed. Reg. 37,286, 37,319 (June 19, 2020).

[154] 85 Fed. Reg. 37,286, 37,292 (June 19, 2020).

[155] 42 C.F.R. § 447.510(b)(1).

[156] 85 Fed. Reg. 37,286, 37,301 and 37,321 (June 19, 2020).

We appreciate the flexibility this change would afford manufacturers entering VBAs. PhRMA thanks CMS for its attention to this issue and supports the proposal, provided that the extended restatement period is voluntary and applies only to VBAs. Further, PhRMA encourages CMS to allow manufacturers to make these VBA-related restatements at any time (including after the 3-year period), without requiring CMS approval.

4. PhRMA Generally Supports, and Suggests Clarifications to, The Proposed Definition of "Value Based Purchasing Arrangement"

CMS proposes the following definition for "value-based purchasing (VBP) arrangement":

> …an arrangement or agreement intended to align pricing and/or payments to an observed or expected therapeutic or clinical value in a population (that is, outcomes relative to costs) and includes, but is not limited to:
>
> (1) Evidence-based measures, which substantially link the cost of a drug to existing evidence of effectiveness and potential value for specific uses of that product.
>
> (2) Outcomes-based measures, which substantially link payment for the drug to that of the drug's actual performance in patient or a population, or a reduction in other medical expenses.[157]

PhRMA generally supports this proposed definition and offers several clarifying suggestions. First, as noted above, we believe "value based arrangement" (or VBA) is a more appropriate term to describe this concept, and we request that the definition make clear that VBAs are voluntary arrangements between manufacturers and payors or provider-based purchasers (or other entities). We also suggest that the definition be crafted with sufficient flexibility to reflect the fact that VBAs' clinical or health outcomes can include a variety of hard clinical endpoints (*e.g.*, reduction in symptoms or improved survival, or reduced patient discontinuation of therapy), valid surrogate endpoints such as biomarkers, or patient adherence, or other health-related outcomes such as reduction in hospitalization or improvement in patient quality of life or productivity. Finally, we caution CMS against establishing a rigid threshold for linking payment or cost for the drug to outcomes or evidence, as this could unintentionally impede implementation of more VBAs; therefore, we suggest that CMS take the word "substantially" out of the proposed definition. We would be happy to follow up with CMS to discuss further changes to the proposed definition.

5. CMS Should Promulgate Another Proposed Rule Addressing its Proposal Concerning Multiple Best Prices

CMS proposes to amend its best price regulation to provide that best price "may include varying best price points for a single dosage form and strength as a result of a VBA."[158] Although CMS does not include any other proposed regulatory text concerning this change,

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[157] 85 Fed. Reg. 37,286, 37,319 (June 19, 2020).

[158] 85 Fed. Reg. 37,286, 37,320 (June 19, 2020).

CMS has some discussion of the proposal in its regulatory preamble. According to the preamble, as an example, a manufacturer implementing a VBA "would report a single best price for the drug for the quarter" as well as "a distinct set of 'best prices' that would be available based on the range of evidence-based or outcomes measures for that drug that are possible under the [VBA]."[159]

Given the lack of proposed regulatory text and the vagueness of the preamble, PhRMA members had a range of questions about this proposal, including but not limited to:

- Are we correct in assuming that if an existing or future arrangement falls into the definition of a VBA, the multiple best price approach is voluntary—*i.e.*, the manufacturer could instead use the bundled sale approach, or another approach that works to even out potential best price impacts?

- In the proposed rule preamble, CMS refers to states "participating" in VBAs and writes that in one example of a VBA, "[t]he calculated MDRP rebate due to the state using the [VBA] best price would be a function of whether or not the Medicaid rebate is being paid on a unit of a drug dispensed to a Medicaid patient that participated in a VBA, and the level of rebate associated with that patient's outcome. . . . Otherwise, the best price used in the Medicaid rebate formula would mirror the lowest price available absent a [VBA]."[160] Could CMS explain how a state Medicaid program would "participate" in a VBA? We are concerned that (among other things) the state reporting that CMS may envision could be difficult for states to generate.

- How would the multiple best price approach apply in situations where manufacturers are testing more than one VBA model for the same product with commercial payors?

- Could a manufacturer terminate a state Medicaid agency's participation in a VBA?

- How could CMS and states learn about VBAs that a manufacturer has with a commercial payor? We would be concerned about the creation of any national database containing proprietary information about VBAs.

- Does CMS intend for a state to enter into a separate agreement with a manufacturer to participate in a VBA? If so, would the state Medicaid program have the same obligations as a commercial plan that entered into the VBA with the manufacturer? How would CMS monitor a state's obligations under a VBA?

- How would CMS update the Drug Data Reporting system (DDR) and other relevant systems in order to operationalize VBAs?

[159] 85 Fed. Reg. 37,286, 37,293 (June 19, 2020).

[160] 85 Fed. Reg. 37,286, 37,293 and 37,321 (June 19, 2020) (emphasis added).

- Is CMS working with the HHS OIG to help ensure that OIG develops guidance that provides flexibility and clarity for a wide range of VBAs and other innovative contracts?

In addition to these questions, we would like to understand the implications of CMS' proposal for the 340B program, given the impact of best price on the Medicaid unit rebate amount, one of the metrics in calculating a drug's 340B ceiling price. As PhRMA has written elsewhere,[161] and as studies by industry experts and government agencies have concluded,[162] for many years now the 340B program has grown at a significant rate, uncontrolled and without proper oversight, without any guarantee the program is benefiting patients. The program urgently needs reforms in order to provide discounted medicines to the vulnerable and uninsured patients it was intended to help and to stop program abuses, including the diversion and duplicate discounting that the 340B law prohibits. Without information on how CMS' multiple best prices proposal would affect 340B,[163] manufacturers cannot assess or comment fully on CMS' proposal.

We continue to support VBAs and appreciate CMS recognizing the importance of these arrangements in the proposed rule. However, we are unable to comment fully on the section of the proposed rule regarding multiple best prices, as this section lacks sufficient information for us to understand the proposed approach and formulate informed comments. Consequently, we ask that CMS not finalize this section and instead promulgate another proposed rule with additional information that fleshes out the multiple best prices proposal, addresses the questions above, and enables commenters to develop meaningful comments on this approach.

D. State-Related Proposals[164]

1. CMS-Authorized Supplemental Rebate Agreements

[161] See PhRMA, Advocacy: 340B (last visited July 3, 2020), available at https://www.phrma.org/en/Advocacy/340B.

[162] E.g., U.S. Government Accountability Office, 340B DRUG DISCOUNT PROGRAM: Oversight of the Intersection with the Medicaid Drug Rebate Program Needs Improvement (Jan. 27, 2020), available at https://www.gao.gov/assets/710/703966.pdf; Adam Fein, New HRSA Data: 340B Program Reached $29.9 Billion in 2019; Now Over 8% of Drug Sales, Drug Channels (June 9, 2020), available at https://www.drugchannels.net/2020/06/new-hrsa-data-340b-program-reached-299.html ("the 340B program is now 85% . . . as large as the Medicaid program.").

[163] For example, the 340B ceiling price is equal to the AMP minus the Medicaid unit rebate amount (URA) for a covered outpatient drug, where the URA calculation hinges significantly on best price. Any change to the best price calculation could, in turn, affect the calculation for a product's 340B ceiling price.

[164] As noted in section C., the type of agreement termed a "value based purchasing" (VBP) arrangement in the proposed rule generally involves manufacturer arrangements with payors rather than purchasers. To clarify that these arrangements are not limited to purchasers, we suggest changing the term to "value-based arrangement" (VBA) rather than "VBP" and therefore we use VBA consistently in section C. In this section D., we also use the term "VBA" to refer to VBAs between manufacturers and State Medicaid programs that take the form of SRAs, as the same point applies here (State Medicaid agencies are payors, so the terminology should not be limited to (continued…)

PhRMA recommends that CMS revise its proposed definition of "CMS-authorized supplemental rebate agreement" to clarify that rebates may fall within this definition regardless of their amount. Under CMS' proposed language, the "supplemental drug rebate arrangements [must] generate rebates that are at least as large as the rebates set forth in the Secretary's national rebate agreement with drug manufacturers." We assume that CMS means that the combined rebates paid under the supplemental rebate agreement (SRA) and the national rebate agreement must be at least as large as the rebates required under the national rebate agreement alone. However, as drafted, this language could be interpreted to mean that the rebates under the SRA itself must equal or exceed the rebates paid under the national drug rebate agreement. We do not believe that this is the result that CMS intended. States' SRAs generally do not displace manufacturers' obligations under the national rebate agreement; instead, they impose additional voluntary rebate obligations.

It is also possible that CMS' proposed language could be construed to mean that every supplemental rebate agreement must result in a positive rebate to the state in every quarter. This reading would also conflict with current practices. Many SRAs use a guaranteed net unit price (GNUP) structure, under which the manufacturer guarantees that the state will pay no more than a certain price for a drug, once both the statutory and supplemental rebates are taken into account. Since the supplemental rebate is dependent on the amount of the statutory rebate and the amount of the statutory rebate is not known with certainty at the time the agreement is executed, in some cases the state receives the guaranteed price based on the statutory rebate alone and therefore a smaller or no supplemental rebate is paid during the applicable quarter. These agreements are still valuable to both states and manufacturers; however, both because they give assurance to states that they will pay no more than a given price and because of the non-financial benefits that accompany such SRAs, such as agreement on coverage criteria that would apply to the applicable drug(s). Similarly, VBAs can also result in zero supplemental rebates being paid to a state in a particular quarter if a drug performs and the applicable outcome measures are met; and these SRAs remain valuable to states because they reduce uncertainty about pharmaceutical product effectiveness and still allow for potentially significant rebates if applicable outcomes are not met in other quarters.

We therefore suggest that CMS revise this definition to clarify that an SRA may be approved by CMS so long as the combined rebate payment under the SRA and national rebate agreement is greater than or equal to the rebate under the national rebate agreement alone. We recommend that CMS revise the first sentence of the definition as follows: "CMS-authorized supplemental rebate agreement means an agreement that is approved through a state plan amendment (SPA) by CMS, which allows a state to enter into single and/or multi-state supplemental drug rebate arrangements that **may** generate rebates **in addition to** ~~that are at least as large as~~ the rebates set forth in the Secretary's national rebate agreement with drug manufacturers." While CMS cited to section 1927(a)(4) in proposing the "at least as large as" language, that paragraph applies in cases where a state seeks to enter into a rebate agreement *in lieu of* a national rebate agreement, not a supplemental rebate agreement authorized by CMS pursuant to section 1927(a)(1) that exists alongside a national rebate agreement. Therefore, such

purchasers). We note also that some of these VBA SRAs involve arrangements that might be seen as going beyond the proposed definition of "value-based purchasing" in section C. (i.e., the proposed definition focuses on evidence-based and outcomes-based arrangements, so may not encompass, for example, pay-over-time SRAs).

paragraph does not dictate the inclusion of language on a minimum rebate amount in the SRA definition.

PhRMA also urges CMS to ensure that states adhere to the requirement to obtain CMS approval prior to implementing changes to SRAs. In its discussion of "CMS-authorized Supplemental Rebate Agreements," CMS notes that states must file a State Plan Amendment (SPA) to reflect such agreements. CMS further refers to its 2002 guidance that discusses the need for federal approval of certain aspects of SRAs.[165] We note, however, that some states have not been adhering to CMS requirements to obtain necessary federal approval of modifications to their supplemental rebate and prior authorization programs. We therefore request that CMS reinforce the need for states to obtain CMS approval prior to implementing changes to supplemental rebate policies.

As CMS recognized in its 2002 guidance, federal regulations require that each state Medicaid plan "must provide that it will be amended whenever necessary to reflect . . . [m]aterial changes in State law, organization, or policy, or in the State's operation of the Medicaid program."[166] States must submit proposed SPAs to CMS after each such material change. "Prompt submittal of [SPA]s is necessary . . . [s]o that CMS can determine whether the plan continues to meet the requirements for approval."[167] CMS has 90 days from the date of submission to approve or reject an SPA (though that time period is extended should CMS request more information from the State).[168] This is an important substantive requirement because it is the only way for CMS to ensure that state Medicaid plans comport with federal requirements.[169]

Yet states often do not seek federal approval when they make material modifications to their supplemental rebate or prior authorization programs. The implementation of New York's Medicaid Prescription Drug Spending Cap (drug cap) law demonstrates how states ignore the regulation. The drug cap statute was enacted in 2017,[170] and New York has never received approval of a SPA related to the law, despite the law imposing numerous material changes to the state's supplemental rebate and prior authorization programs, including:

- Imposing new access restrictions on drugs in cases where the manufacturer does not agree to provide the target supplemental rebate, including imposing prior authorization on the drug for the first time or eliminating the state's "prescriber prevails" rule (which allows the prescriber to ultimately decide whether the beneficiary has access to the drug).

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[165] CMS, State Medicaid Director Letter No. 02-014 (Sept. 18, 2002), available at https://www.medicaid.gov/sites/default/files/Federal-Policy-Guidance/downloads/smd091802.pdf.

[166] 42 C.F.R. § 430.12(c)(1)(ii) (emphasis added).

[167] Id.

[168] 42 U.S.C. § 1396n(f)(2).

[169] But see Cmty. Health Care Ass'n of New York v. Shah, 770 F.3d 129, 148 n.2 (2d Cir. 2014) (calling the State's failure to submit a proposed SPA for approval "procedural shortcoming" in dicta).

[170] N.Y. Pub. Health Law § 280.

- Reducing Medicaid managed care reimbursement and coverage of a drug if a manufacturer does not agree to provide the target supplemental rebate.
- Linking requests for supplemental rebate negotiation to drug price transparency disclosures provided by manufacturers.
- Changing the responsibilities and membership qualifications of the state's Drug Utilization Review Board (DURB) so that the DURB can now conduct economic analyses of the value of drugs and recommend the amount of a target supplemental rebate. Since no SPA was filed, the description of the DURB in the state plan is outdated and does not reflect the actual responsibilities of the DURB under current law.

Further, New York did not seek a SPA even though the state (1) publicly indicated it would file such a SPA prior to implementing the new law,[171] and (2) did file a SPA prior to using its powers under the state's global spending cap, a statute similar to the prescription drug cap. Without consistent enforcement by CMS, other states may follow New York's lead and decline to seek federal approval when adopting similar policies in violation of CMS' requirements.

States should not be able to implement such substantial shifts in their operations without federal approval. As CMS is well aware, the requirement to obtain federal approval is not simply a check-the-box exercise, but an important safeguard for Medicaid beneficiaries. As in the case of New York, these policies can reduce beneficiary access to needed medications through the removal of drugs from preferred drug lists, the imposition of prior authorization, the ending of prescriber prevails policies, or via other means. The end result is that a beneficiary who has long taken a particular medication may face additional barriers to remain on such medication or may be forced to switched to a different drug altogether. CMS should ensure that states obtain federal approval before implementing programs that can have material changes on the way Medicaid beneficiaries access drugs. We therefore respectfully request that CMS better enforce its current guidance to states regarding submission of a SPA to CMS prior to implementing changes to the state's supplemental rebate policies.

2. Data Requirements for States

We support CMS' goal of requiring states to provide more accurate data related to the MDRP, and we agree with CMS' proposal to improve the quality of data reported by states under § 447.511. However, CMS should also mandate that states provide claims-level data as a means of ensuring the accuracy of their calculations and reporting.

As CMS acknowledges in the proposed rule, states sometimes overbill manufacturers because they have not put sufficient edits in place to detect claims that should not be paid. Neglecting to correct these errors results in manufacturers understandably disputing the rebates invoiced to them, which can lead to the parties turning to the state hearing process or the alternative dispute resolution process to resolve the disagreement. These can be timely and costly processes for both states and manufacturers.

[171] 39 N.Y. State Reg. 19, at 142-43 (May 10, 2017), available at https://docs.dos.ny.gov/info/register/2017/may10/pdf/Miscellaneous.pdf.

In order to address overbilling of rebates and other concerns related to the integrity of state data, CMS proposes that states should ensure that CMS receives the same information that is provided to manufacturers on the CMS-R-144. Further, CMS proposes that a state must certify that "it has applied any necessary edits to the data for both CMS and the labeler to avoid inaccuracies at both the NDC/line item and file/aggregate level." These new requirements are a step in the right direction. However, they will not resolve the inaccuracies of state data. States still lack a clear incentive to ensure that their edits are sufficient to flag improper claims, particularly since it takes resources to develop and apply those edits.

We believe that CMS should go further to improve the integrity of state data and require states to provide claim-level data to both manufacturers and CMS in conjunction with state invoices. States should be required to report data at a claim level and share claims-level data with manufacturers. Such data will help states comply with their obligations to prevent duplicate discounts under the 340B program, unit of measure (UOM) discrepancies, and other common data errors. CMS has already recognized that claims-level data can play an important role in addressing state data inaccuracies, as the agency has encouraged states to respond to reasonable manufacturer requests for such data.[172] A recent GAO report found that the procedures that states use to exclude 340B drugs from Medicaid rebate requests are not always documented or effective at identifying these drugs.[173] GAO also found that when duplicate discounts occur, manufacturers may have little ability to recover inaccurate payments. Like GAO, OIG has identified claim-level data methods as a way states can more accurately identify 340B claims and thus reduce the risk of duplicate discounts and forgone rebates associated with provider-level methods.[174]

The provision of such data will ultimately result in administrative efficiencies in the MDRP for both manufacturers and states. While states may incur some initial costs in establishing processes to provide such data, ultimately the sharing of claims-level data will result in more accurate invoices billed to manufacturers and therefore less time, energy, and resources spent on the dispute resolution process.

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[172] CMS, Medicaid Drug Rebate Program Notice Release No. 173 (Dec. 31, 2015), available at https://www.medicaid.gov/Medicaid-CHIP-Program-Information/By-Topics/Prescription-Drugs/Downloads/Rx-Releases/State-Releases/state-rel-173.pdf.

[173] Government Accountability Office, 340B Drug Discount Program: Oversight of the Intersection with the Medicaid Drug Rebate Program Needs Improvement (Jan. 21, 2020) available at https://www.gao.gov/products/GAO-20-212.

[174] Department of Health and Human Services Office of Inspector General, State Efforts to Exclude 340B Drugs from Medicaid Managed Care Rebates (June 2016), available at https://oig.hhs.gov/oei/reports/oei-05-14-00430.pdf.

3. State Plan Requirements, Findings and Assurances

As we stated earlier in this letter, we support CMS' efforts to give manufacturers and payors more flexibility in engaging in VBAs, and we share the agency's commitment to ensuring that Medicaid programs benefit from VBAs entered into by states. We also appreciate the agency's desire to provide ongoing monitoring and oversight of VBAs implemented between manufacturers and state Medicaid programs. PhRMA believes that these efforts are an important first step in supporting a health care market that demands accountability and ensuring that both patients and payors benefit from VBAs.

However, with regard to the additional reporting requirements proposed for states, we urge CMS to carefully evaluate these requirements and ensure that any potential benefit is commensurate with the added burden placed on states. Specifically, with respect to state reporting of VBAs, we urge CMS to reconsider whether it is appropriate to impose a new obligation on states to provide the costs to administer VBAs and the savings resulting from such arrangements, and that CMS decline to adopt other reporting obligations associated with VBAs. CMS should also ensure that any information provided by states is subject to the confidentiality obligations of section 1927 and that any confidential and proprietary information reported by the state will not be redisclosed by CMS.

While savings under some VBAs can be calculated easily, other arrangements may involve more difficult calculations. As CMS has acknowledged, many VBAs may involve measuring outcomes over months or years so reporting that would take place annually may fail to provide an accurate measure of the total savings. Even in the case of one-year VBAs, outcomes may not be determined within 60 days of year's end, CMS' proposed reporting deadline. The data element requiring states to report the "total savings generated by the supplemental rebate due to the VB[A]" may underestimate savings due to failure to account for rebates that have yet to be paid. Comparing costs to savings in these scenarios may lead to the incorrect conclusion that states are not benefiting from VBA efforts.

If CMS were to move forward with the proposed reporting elements, CMS should provide guidance to states to ensure the accuracy and consistency of state calculations of the required elements. For example, CMS should explain how states should estimate savings that have not been determined as of the reporting deadline. CMS also should ensure there is an opportunity for public comment prior to issuing any guidance on methodologies for determining costs and savings. In addition, a manufacturer that enters a VBA with a state should have the opportunity to review and comment on a draft of the state's annual reporting on the results of the VBA prior to the state submitting it to CMS. Given the complexity and novelty of the savings calculation that may be necessary for this reporting, CMS should require that both parties to the VBA agree on its outcomes.

For now, CMS should require state reporting of only the basic data needed to understand the magnitude of VBAs: the drugs subject to VBAs and the number of units dispensed under such arrangements. CMS should not expand the types of data states would be required to report under VBAs to CMS (such as other indirect costs or clinical or other patient-related outcomes). These other data elements are often much more challenging to measure under VBAs. Requiring such reporting by states would significantly increase administrative burden and increase the risk that inaccurate data are reported.

In addition, if the VBA reporting requirements are finalized in any form, CMS should clarify that such reports are subject to the confidentiality restrictions set forth in the MDRP statute at Section 1927(b)(3)(D) and that any confidential and proprietary information reported by the state will not be redisclosed by CMS. Even if identifying information related to particular drugs and manufacturers were removed from public reports, data on the amount of savings and other aspects of VBA design could be used to determine a manufacturer's VBA pricing, particularly if there are a small number of VBAs in certain states. We therefore urge CMS to include within §447.518(d) a reference to the confidentiality obligations at Section 1927(b)(3)(D). We also request that the agency work with states to ensure that any VBA reporting complies with these confidentiality requirements.

E. New Medicaid Drug Utilization Review (DUR) Provisions Designed to Reduce Opioid Related Fraud, Misuse and Abuse

1. Implementation of SUPPORT for Patients and Communities Act (SUPPORT Act) Provisions

Section 1004 of the SUPPORT Act (the Act) requires states to implement certain opioid specific DUR standards in Medicaid fee-for-service (FFS) and in Medicaid managed care plans. Specifically, the Act requires states to implement opioid related prospective safety edit alerts (prospective DUR) and automatic retrospective claims review (retrospective DUR) for opioids as part of each state's respective DUR programs. In the proposed rule, CMS proposes minimum standards for opioid-related DUR programs to ensure a consistent baseline for DUR activities in the states. In addition to the opioid-specific prospective and retrospective DUR requirements, CMS is proposing to codify SUPPORT Act provisions which require states to implement (1) retrospective DUR to monitor concurrent opioid use with benzodiazepines as well as with antipsychotics and (2) requirements for states to establish processes to identify fraud and abuse of controlled substances. Additionally, the Act requires that states be required to implement programs to monitor and manage the appropriate use of antipsychotic medications by children enrolled under the state plan, including any Medicaid expansion groups or the Children's Health Insurance Program.

PhRMA supports the use of appropriate means to address misuse, abuse and potentially problematic utilization of prescription drugs, which can endanger patients' safety, health and also increase costs to the health care system through increased utilization of other health care services such as through avoidable emergency room visits and hospitalizations. We also appreciate CMS' work to assure that efforts aimed at curbing overutilization of controlled substances do not become unduly restrictive or impede patient access to medically necessary drugs, particularly for patients with chronic pain, patients in hospice, or patients with cancer diagnoses. Inappropriately restricting access, particularly for vulnerable low-income populations, may have negative consequences for Medicaid beneficiaries, and we trust that CMS is cognizant of the need to guard against these risks.

Over the years, PhRMA has expressed support for efforts to ensure health plans monitor and seek to prevent inappropriate prescribing and use through DUR and quality assurance programs. As CMS moves forward with implementing opioid-specific DUR standards mandated

by the SUPPORT Act, we believe these DUR programs should be informed by a thoughtful and evidence-based approach guided by clinical guidelines and validated measures of inappropriate levels of utilization.

For example, meaningful and effective DUR activities should assure individuals flagged by DUR activities get the care they need while also acknowledging the complexity of the care required by many of these patients. To inform appropriate interventions, we believe clinical contact with prescribers and relevant care management teams is a critical component of any successful DUR program. Many of those who would be flagged through DUR activities—particularly those who may be prescribed opioids along with other classes of medications—are patients who lack coordinated care, may be at risk for adverse events or may benefit from medical intervention to address polypharmacy issues, substance use and/or mental health disorders. Accordingly, DUR programs should be designed not solely around preventing fraud and abuse but rather to provide critical communication with prescribers who may otherwise be uniformed about the need for appropriate intervention. Likewise, it is critical that clinical contact is made with providers to verify outlier utilization which may be entirely appropriate, particularly for those with complex pain management issues and co-morbid conditions.

We appreciate CMS' recognition of the importance that states utilize retrospective DUR to continually refine measures which inform prospective safety edit alerts at the point of sale. As states move forward with implementing minimum DUR standards, we believe continued refinement of the criteria that states define for the purposes of identifying potentially inappropriate levels of opioid overutilization will help to ensure these programs successfully prevent misuse and abuse while also ensuring patients with complex chronic pain conditions are not unnecessarily limited in their ability to access needed care. We encourage CMS to review annual reports submitted by states with regards to DUR activities with an eye towards ensuring the validity of measures used to flag potentially inappropriate levels of utilization and to support continued refinement.

With respect to the minimum standards proposed in the rule, we appreciate that CMS is not seeking to establish a minimum floor for the purposes of determining appropriate opioid utilization. However, we are concerned that states may apply a one-size-fits all approach in establishing these limitations. PhRMA supports the development and use of guidelines to inform appropriate prescribing for the treatment of pain, including the *CDC Guideline for Prescribing Opioids for Chronic Pain.*[175] These guidelines were developed for the purposes of providing primary care clinicians with guidance on managing chronic pain with opioid pain relievers; however, the misapplication and misinterpretation of the guidelines has led to unintended consequences, particularly for chronic pain patients. Unfortunately, as noted in the rule, there

[175] Deborah Dowell, et al., CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016, 65 Morbidity and Mortality Wkly. Rep. 1, at 1-49 (2016), available at https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm.

have been well documented adverse events associated with the broad application of these guidelines beyond the intended treatment population.[176]

In recognition of these challenges, CDC has sought public comment from acute and chronic pain patients, patients' family members and/or caregivers and health care providers who care for patients with pain or conditions that can complicate pain management, including opioid use disorder (OUD) and risk of overdose.[177] As the CDC assesses this stakeholder input and continues to reevaluate updating and expanding its guidelines we appreciate continued flexibility to ensure this stakeholder input is accounted for in future policies aimed to curb inappropriate opioid utilization and improve the treatment of pain.

To help further the development of clinical guidelines, we encourage CMS to work with various stakeholders, including NIH and NIDA, to develop objective measures of pain and to perform ongoing assessment of the DUR activities to ensure that legitimate patient access to appropriate pain treatment is not negatively impacted. Additionally, we encourage HHS agencies, particularly CMS, to continue to support the development and dissemination of evidence based clinical guidelines by medical sub-specialties to inform appropriate prescribing, particularly for treatment populations with complex pain management issues, and to help serve as a tool for the treatment of chronic pain.

With respect to efforts to implement SUPPORT Act requirements related to implementing programs to monitor and manage antipsychotic use in children, we feel the same aforementioned principles should also inform state activities in implementing these requirements. We agree with CMS' statement that these proposed provisions are not meant to prohibit the exercise of clinical judgment by a provider regarding the best or most appropriate care and treatment for any patient. We also believe these programs should align with national clinical practice guidelines and that it is important for ongoing monitoring to ensure state DUR activities are not impeding legitimate and appropriate access to needed medications.

2. Establishing and Encouraging Minimum Safety Standards for Medicaid DUR Programs beyond SUPPORT Act Requirements

In addition to implementing DUR requirements established in the SUPPORT Act, CMS is taking steps to enhance Medicaid DUR programs by establishing minimum safety standards to ensure safe use among those with OUD and those who may be at risk for opioid overdose. Specifically, state DUR programs would be required to have safety edits (prospective DUR), a retrospective DUR program or some combination of these approaches to identify:

- Medicaid beneficiaries prescribed an opioid after one or more drugs are prescribed for medication-assisted treatment (MAT) or beneficiaries who had an OUD diagnosis within a specified number of days, without having a new indication to support utilization of opioids (*e.g.*, cancer, new palliative care treatment or entry into hospice).

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[176] Jeffrey Fudin, et al., Safety Concerns with the Centers for Disease Control Opioid Calculator, 11 *J. of Pain Res.* 1, at 1-4 (2018), available at https://www.dovepress.com/safety-concerns-with-the-centers-for-disease-control-opioid-calculator-peer-reviewed-article-JPR.

[177] CDC, Management of Acute and Chronic Pain: Request for Comment (Apr. 17, 2020), available at https://beta.regulations.gov/document/CDC-2020-0029-0001.

- Medicaid beneficiaries who could be at risk of opioid overdose and should be considered for co-prescription or co-dispensing of naloxone.

PhRMA applauds the additional steps CMS is taking to protect against adverse events among patients with OUD and those who face an increased risk of an overdose. We support a thoughtful and clinically based approach to efforts to ensure safe use among individuals struggling with addiction. Additionally, we encourage an approach which recognizes the significant hurdles these patients face in accessing appropriate addiction treatment. In consideration of these challenges, we encourage measures to ensure patients are not impeded from accessing MAT therapies, particularly given the path to treatment may present some complications for these patients. Ensuring DUR programs are based on well-constructed measures for identifying these individuals can not only help to prevent overdose but support care coordination with addiction treatment providers. Likewise, we support interventions to promote naloxone co-prescribing and dispensing for at risk beneficiaries and believe this is a critical tool to addressing the addiction crisis. We additionally recommend that CMS consider approaches to expand education on administering opioid reversal agents and in recognizing the signs and symptoms of an overdose.

We also applaud CMS' efforts to solicit comments on additional future standards that may be adopted through rulemaking to ensure minimally adequate DUR programs that help ensure prescribed drugs are appropriate, medically necessary, and not likely to result in adverse medical results. We believe broad stakeholder input, particularly from those in the medical community and patient groups will be critical to striking the right balance between curbing unsafe and inappropriate utilization of prescription medicines while also ensuring legitimate access to care is not impeded. For these same reasons we recommend that CMS' consideration of future mechanisms to encourage additional DUR standards for states to respond to the new and emerging issues in drug use outside of rulemaking be limited to standards concerning opioid utilization. We recognize the need to provide swift guidance to states to address the opioid crisis. As guidelines informed by medical and clinical expertise and broad stakeholder input from patients and caregivers regarding the appropriate treatment of acute and chronic pain continue to be revised, developed, and expanded, we believe CMS can play an important role in the dissemination of these guidelines for states to consider in adopting additional minimum DUR standards in clinically appropriate circumstances. Furthermore, we believe CMS can play a role in highlighting best practices for states to consider in expanding or refining DUR programs, such as publishing case studies in innovative DUR approaches proven effective in curbing inappropriate utilization of opioids.

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PhRMA appreciates your consideration of these comments. Please feel free to contact James Stansel at jstansel@phrma.org, Jennifer Bryant at jbryant@phrma.org and/or Sylvia Yu at syu@phrma.org if there is any further information we can provide or if you have any questions about our comments.

Sincerely,

_____/s/_____
James C. Stansel
Executive Vice President and General Counsel

_____/s/_____
Jennifer Bryant
Executive Vice President, Policy, Research
and Membership

_____/s/_____
Sylvia Yu
Vice President, Federal Programs