Applying the Results of Comparative Effectiveness Research to Control Drug Costs: Policy Options for California

White Paper

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About ICER

The Institute for Clinical and Economic Review (ICER) is an independent non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders interpret and apply evidence to improve patient outcomes and control costs. Through all its work, ICER seeks to help create a future in which collaborative efforts to move evidence into action provide the foundation for a more effective, efficient, and just health care system. More information about ICER is available at https://icer.org/.

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List of Acronyms and Abbreviations Used in this Paper

AMP	Average manufacturer price
CBO	Congressional Budget Office
CDL	Contract drug list
CER	Comparative effectiveness research
CPI-M	Consumer price index – medical care
CPI-U	Consumer price index – all urban consumers
DMHC	Department of Managed Health Care
DOI	Division of Insurance
DOH	Department of Health
DUR	Drug Utilization Review
EOHHS	Executive Office of Health and Human Services
ERISA	Employee Retirement Income Security Act
evLYG	Equal value of life years gained
FMAP	Federal medical assistance percentage
HCAI	Department of Health Care Access and Information
HPC	Health Policy Commission
ICER	Institute for Clinical and Economic Review
IRA	Inflation Reduction Act
MCO	Managed care organization
NASHP	National Academy for State Health Policy
P**&**T	Pharmacy and therapeutics
PBGH	Purchaser Business Group on Health
PBM	Pharmacy benefit manager
PDAB	Prescription drug affordability board
PDL	Preferred drug list
PMPM	Per member per month
QALY	Quality-adjusted life year
R&D	Research and development
UPI	Unsupported price increase
UPL	Upper payment limit

Executive Summary

Rising prescription drug spending is a major concern for policymakers in California. In the California Health Care Foundation's 2023 Health Policy Survey, 20% of Californians reported that they did not fill a prescription due to cost, a figure that rises to 33% for individuals who earn less than 200% of the federal poverty level; 16% of Californians reported cutting pills in half or skipping doses to save money.[1] Nationally, 20% of adults who take between one to three prescription drugs have difficulty affording their medications, a number that increases to 32% for individuals who take four or more medications.[2] A December 2022 report from the California Department of Managed Health Care found that health plans in the state paid approximately $10.8 billion for prescription drugs in 2021. This represents $2.1 billion in additional spending compared to 2017, a 22% increase.[3]

In recent years, state policymakers as well as public and private insurers have attempted to rein in prescription drug spending by leveraging the evidence produced by comparative effectiveness research (CER). CER has two complementary components: a comparative clinical effectiveness analysis that compares the relative clinical benefits and disadvantages of different treatment options for a condition, and a cost-effectiveness analysis that compares the modeled estimates of the long-term clinical and economic outcomes for two or more treatment options. These components of CER can be used alone or in combination: clinical comparative effectiveness review can help determine whether drugs offer important clinical benefits over therapeutic alternatives; and if there are additional benefits, cost-effectiveness analysis allows policymakers to determine what a fair price would be for use in price negotiations, formulary design, and other approaches to lower drug costs.

Managed care plans and health care purchasers like the California Department of Health Care Services (DHCS), CalPERS, and large self-insured employers in California are already using elements of CER in their purchasing and coverage decisions. However, interviews conducted for this study suggest several opportunities for public and private entities to further utilize CER to address drug costs.

This white paper has been developed by staff of the Institute for Clinical and Economic Review (ICER), an independent non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders interpret and apply evidence to improve patient outcomes and control costs. To inform this paper, ICER conducted interviews with representatives from California state agencies, public and private payers in California, experts on drug pricing policy, and individuals from other states who are involved in efforts to manage drug spending. In order to promote candor, we do not identify any of these individuals by name; a list of the organizations these individuals represent is presented in Appendix A.

Potential policy and purchasing options for further aligning prescription drug spending with value in California include:

1. Expanding Prescription Drug Reporting Requirements

California currently requires drug makers to provide list prices for new drugs that exceed Medicare's threshold for specialty drugs and of price increases of greater than 16% for drugs that cost $40 or more for a 30-day supply. The state also requires insurers to report a list of the 25 most frequently prescribed drugs, 25 drugs with the highest annual spending by list price, and the 25 drugs whose spending increases contribute the most to growth in annual plan spending. While this information provides transparency into list prices and the costliest drugs to insurers, it does not allow policymakers to determine a drug's net price, which reflects negotiated discounts and other price concessions. Without this information, it is impossible to determine whether spending increases are driven by net price increases, which may or may not be justified, or by additional utilization, which may be supported by clinical evidence.

State policymakers could consider requiring drug makers to disclose volume data along with pricing, fee, and rebate information across different supply chain entities. Alternatively, payers could provide pricing and volume information, but those data would not include the fees and discounts paid to other parts of the drug supply chain.

Policymakers could use this new information gathered under enhanced reporting requirements to highlight more effectively those drugs whose net prices to public and commercial insurers exceed fair price benchmarks generated by comparative cost-effectiveness analysis. This information could also be used to support further action, such as the imposition of penalties for drug price increases that exceed a certain threshold and/or are introduced without new evidence of improved clinical performance.

2. Establishing State-Based Drug Affordability Review Authority

Several states are exploring—and in some cases, implementing—prescription drug affordability review authority that utilizes CER. These initiatives authorize Medicaid programs to pursue supplemental rebates via an affordability review process and/or create a *de novo* prescription drug affordability board (PDAB) with the authority to set an upper payment limit (UPL) that state (and possibly private) purchasers will pay for a prescription drug. Either approach empowers a state to determine whether the costs of individual drugs are reasonable and, if not, to achieve pricing concessions to improve affordability for payers and patients.

Under the Medicaid-focused approach, an existing Medicaid drug utilization review (DUR) board or other state agency reviews evidence produced by CER to identify a target for supplemental rebate negotiations. New York established a Medicaid drug spending cap that, when pierced, empowers

the state to identify the drugs in the top 3% of Medicaid spending for targeted supplemental rebate negotiations. Since implementing this program in 2017, New York's Medicaid program has saved over $600 million. The program established in Massachusetts authorizes the state's Health Policy Commission (HPC) to convene a public meeting to determine a proposed fair price for drugs on which the state spends more than $10 million per year and those with list prices of greater than $25,000 per year if the state's Medicaid program is unable to reach a supplemental rebate agreement with a drug maker.[4] The prospect of a public meeting has served as an incentive to bring drug makers to the table and achieve deeper supplemental rebates, contributing to an estimated $171 million in savings as of November 2021.

The other state-based approach is to establish a PDAB which is empowered to use evidence from CER to establish an UPL that public (and potentially commercial) insurers may not exceed when purchasing a drug. To date, six states (Colorado, Maryland, Maine, New Hampshire, Oregon, and Washington) have enacted some form of PDAB and are in varying stages of the rulemaking process prior to their first effort to set a UPL.

States that explore prescription drug affordability review authority through Medicaid DUR boards or PDABs should consider safeguard language such as that developed by ICER and used by Washington state that sets standards for the use of the quality-adjusted life year (QALY) or other measures of health improvement in cost-effectiveness analysis to address concerns regarding discrimination against individuals living with chronic disabilities.[5]

3. Expanding the Use of CER to Negotiate Drug Prices and Support Value-Based Benefit Designs

Many health plans in California use fair price calculations from CER to inform price negotiations with drug makers. Anecdotes from the commercial health plan community suggest that the price targets identified by CER serve an important role during negotiations, as drug makers are likely to push for as much as the market will bear no matter how limited the added clinical benefits of their new drug is compared to other options.

Medicaid programs use the clinical effectiveness and cost-effectiveness analyses from CER to inform which drugs are included on their preferred drug lists (PDLs). California's Medicaid agency reports considering independent CER reviews as part of its pharmacy benefit design process.[6] The recently-implemented Medi-Cal Rx program, which has shifted the state's Medicaid prescription drug purchasing away from individual managed care plans to a statewide fee-for-service model, presents policymakers with an opportunity to utilize greater scale in applying CER price benchmarks in negotiation and benefit design.

Covered California could set more explicit standards for participating health plans in the use of CER for drug price negotiation and formulary design. Health plan pharmacy and therapeutics (P&T)

committees could be required to demonstrate how they use evidence produced by CER when determining inclusion in the formulary, and the tiering and specific coverage criteria for each drug. Covered California could also require plans to demonstrate how they consider cost-effectiveness analyses from CER when negotiating drug prices after coverage decisions are made by the P&T committee.

Value-based benefit design is another opportunity for greater use of CER. These benefit designs place clinically effective and appropriately priced drugs on lower tiers with little to no cost sharing for patients. Some commercial payers and state employee programs like CalPERs already pursue this approach, but broader application would create greater incentives for drug makers to negotiate prices aligned with cost-effectiveness analysis. Additional innovative benefit designs that could be developed with application of CER include: 1) "pay-up-to" formularies under which more drugs are included in formularies to enhance patient choice but payment is capped at a fair price maximum determined by CER; 2) "exclusionary formularies" that use both clinical effectiveness and cost-effectiveness analysis to exclude overpriced drugs in favor of fairly-priced alternatives; and 3) "waste-free" formularies under which payers review utilization data in conjunction with CER analyses to identify opportunities to encourage patients to switch to equally effective yet more reasonably-priced drugs when possible.

Conclusion

CER produces information that can guide multiple approaches to assuring that patients have access to the drugs that are appropriate for their clinical situation at an affordable price commensurate with clinical benefit. State policymakers and purchasers have important opportunities to foster the use of CER to achieve this goal. Due to the complexity of the drug supply chain and the natural monopoly many drug manufacturers enjoy, no single policy action aimed at improving value will sufficiently and permanently improve the market for prescription drugs. Nonetheless, state policymakers and purchasers in California are uniquely positioned to consider a number of steps to further integrate CER into insurance benefit design, formulary development, and price negotiation to drive progress in achieving a health care system that can guarantee fair pricing, fair access, and future innovation.

1. Introduction

Rising prescription drug spending is a major concern for policymakers in California. In the 2023 CHCF California Health Policy Survey, 20% of Californians reported that they did not fill a prescription due to cost, a figure that rises to 33% for individuals who earn less than 200% of the federal poverty level; 16% of Californians reported cutting pills in half or skipping doses to save money.[1] Nationally, 20% of adults who take between one to three prescription drugs have difficulty affording their medications, a number that increases to 32% for individuals who take four or more medications.[2] A December 2022 report from the California Department of Managed Health Care found that health plans in the state paid approximately $10.8 billion for prescription drugs in 2021. This represents $2.1 billion in additional spending compared to 2017, a 22% increase.[3]

In recent years, states and commercial payers have attempted to rein in prescription drug spending through several approaches. Many states have enacted transparency laws that requires drug makers to report the prices and price increases for their products; these laws are intended to increase public awareness of drug prices and to discourage drug makers from excessive price hikes. A growing number of states are pursuing some form of prescription drug affordability review authority, under which the state conducts a public review of information on a drug's clinical and economic benefits and uses those data to determine a target price for the drug; these prices are then used to support supplemental rebate negotiations for Medicaid programs or as upper limits to the amount that all payers in the state may pay for the drug. Public and commercial payers have also begun using evidence of a drug's value to inform formulary and benefit design, with the goal of encouraging patients to choose high-value treatments and to increase pressure on drug makers to choose more affordable prices for their products.

In this paper, we explore the potential actions that public and private payers, purchasers, and policymakers in California can take to address drug costs by leveraging evidence produced by comparative effectiveness research (CER). CER has two complementary components. First, comparative clinical effectiveness analysis compares the relative clinical benefits and disadvantages of different treatment options for a condition, often merging data from numerous studies. The second component of CER, comparative cost-effectiveness analysis, compares the modeled estimates of the long-term clinical and economic outcomes for two or more treatment options. These components of CER can be used alone or in combination: clinical comparative effectiveness review can help determine whether drugs offer important clinical benefits over therapeutic alternatives; and if there are additional benefits, cost-effectiveness analysis allows policymakers to determine what a fair price would be for use in price negotiations, formulary design, and other approaches to address high drug costs.

Due to the complexity of the drug supply chain and the natural monopoly many drug manufacturers enjoy, no single policy action aimed at improving value will sufficiently and permanently improve

the market for prescription drugs. Nonetheless, policymakers, payers, and purchasers in California find themselves uniquely positioned to consider a number of steps to further integrate CER into the design of health benefits and drug formularies, and to leverage this research to strengthen drug price negotiation. In subsequent sections of this paper, we present a series of potential policy and purchasing actions, exploring the elements most needed for their success in the context of California's current policy and health system environment.

Authors and Methods

This white paper has been developed by staff of the Institute for Clinical and Economic Review (ICER), an independent non-profit research organization that evaluates medical evidence and convenes public deliberative bodies to help stakeholders interpret and apply evidence to improve patient outcomes and control costs. Through all its work, ICER seeks to help create a future in which collaborative efforts to move evidence into action provide the foundation for a more effective, efficient, and just health care system. With regard to prescription drugs, we believe that when drug prices are fairly aligned with value, payers should remove barriers to access, patients will be able to afford health care, and drug makers will still be rewarded for innovation.

To inform this paper, ICER conducted interviews with representatives from California state agencies, public and private payers in California, experts on legislative considerations for drug pricing policy, and individuals from other states who are involved in efforts to manage drug spending. In order to promote candor, we do not identify any of these individuals by name; a list of the organizations these individuals represent is presented in Appendix A. None of these individuals is responsible for the final contents of this white paper, nor should it be assumed that they support any part of it. The paper should be viewed as attributable solely to the ICER authors.

Background: The Drug Delivery Supply Chain and Rebates

The Drug Delivery Supply Chain

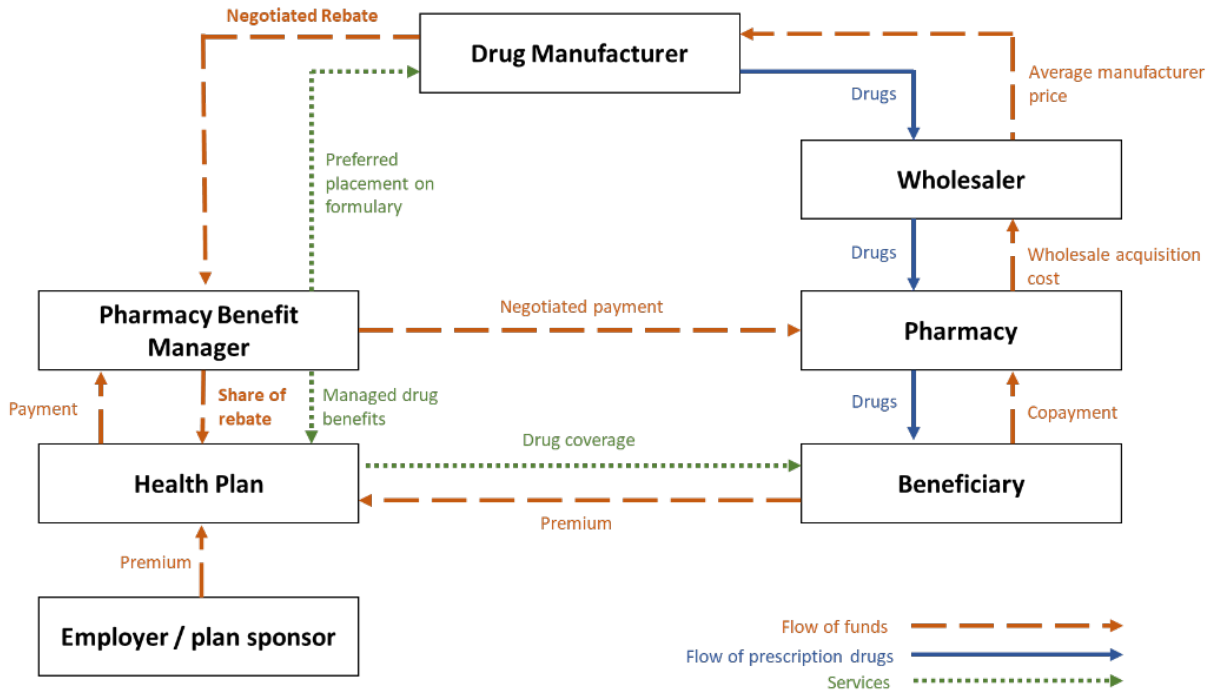
Drug makers in the US face no federal process whereby prices are evaluated in comparison to evidence of clinical benefit, but they must negotiate with a myriad of payers, including both health insurers and pharmacy benefit managers (PBMs). Negotiated discounts to the list price of drugs, rendered post-sale as rebates, help produce lower net prices for drugs, reducing the overall costs of drug spending. But for many years the PBM business model has included a revenue stream gained by retaining a percent of the absolute rebate amount returned to employers or other plan sponsors.

Even though most PBMs have shifted largely to taking a flat fee per prescription rather than a percentage of the rebate as revenue, many believe that the profitability of rebates to PBMs continues to provide an incentive to favor drugs with high list prices and large rebates that might

not be the lowest net cost option.[7] Higher list prices harm patients without insurance, and even patients with insurance pay their out-of-pocket deductible or co-insurance amounts based on the list price of a drug, not the negotiated (and confidential) price net of rebates.[8-10]

Rebates and fees play an important role throughout the complex supply chain for prescription drugs in the US. The following figure illustrates the flow of services, products, and payments (including rebates).

Figure 1. Simplified Illustration of the Flow of Products, Payments, and Services in the Pharmaceutical Supply Chain



Source: Illustration based on Congressional Budget Office[11]

Medicaid Drug Rebates

By law, drug makers must enter into a Medicaid drug rebate agreement with the Department of Health and Human Services if they want their drugs to be covered by the program, a requirement meant to balance out Medicaid's obligation to cover nearly all prescription drugs.[12-14] For most brand drugs, Medicaid programs receive rebates of 23.1% off the average manufacturer price (AMP) or an even deeper rebate to match the "best price" offered to any commercial payer. Brand drugs approved only for pediatric indications and some clotting factors receive a smaller minimum rebate of 17.1% or that needed to meet the best commercial price. Generic drugs are subject to an automatic 13% rebate off AMP, without consideration of the best price available to other payers.

There is an additional Medicaid rebate added on when a drug's price increases beyond the general rate of inflation for urban consumers.[13]

These statutory rebates are split between the federal and state government regardless of whether prescription drugs are provided under a fee-for-service arrangement or by managed care organizations (MCOs). The proportion that the federal government receives is tied to the amount of Medicaid funds provided by the federal government; as a result, the size of the federal portion can fluctuate over time.[12-14] State Medicaid agencies and MCOs may also negotiate supplemental rebates beyond the mandatory rebates just described; these rebates do not factor into the calculation of best price for Medicaid programs in other states. As with statutory rebates, supplemental rebates are split between the federal and state government.[15] Supplemental rebates for individual drugs are typically negotiated as a guaranteed net price and, as such, if the federal share of the statutory rebate increases, the amount of the supplemental rebate retained by the state or MCO decreases, and vice versa.[14]

As of June 2022, 47 states (including California) and the District of Columbia participate in supplemental rebate arrangements.[16] Nationally, Medicaid agencies reported a total of $80.6 billion in gross spending and $42.5 billion in total rebates ($39.7 billion in statutory rebates and $2.8 billion in supplemental rebates) during fiscal year 2021.[17] California reported $8.5 billion in gross spending and $4.5 billion in total rebates ($4.4 billion in statutory rebates and $102.6 million in supplemental rebates) during the same period.[18,19] States do not disclose supplemental rebate amounts for individual drugs because they are achieved, in part, by agreeing to keep the amount confidential.

Most states have also developed a preferred drug list (PDL) as one method of securing supplemental rebates. Medicaid programs may negotiate supplemental rebates in exchange for preferred status on the PDL (i.e., removing or reducing prior authorization requirements) which makes it easier for beneficiaries to access a given drug. The California Department of Health Care Services (DHCS) manages the state's PDL, which is called the "contract drug list" (CDL). Drugs on the CDL are typically those for which DHCS has negotiated a supplemental rebate agreement and are not subject to prior authorization requirements. Drugs excluded from the CDL require prior authorization. DHCS considers a range of evidence when determining whether to add or remove a drug from the CDL, including safety, effectiveness, need, potential for misuse, and the cost of the drug to Medi-Cal. In addition, DHCS seeks input from the Medi-Cal Drug Advisory Committee, which is composed of physicians, pharmacists, faculty from academic pharmacy institutions, and Medi-Cal beneficiaries.[20]

On January 1, 2022, California began implementation of the Medi-Cal Rx program, which shifted the program's pharmacy benefit from MCOs to a fee-for-service model managed by DHCS and Magellan Health. Among other goals, the transition is intended to improve California's ability to negotiate supplemental rebates by bringing all Medi-Cal pharmacy claims under the fee-for-service model,

whereas the previous model left most negotiations to individual managed care organizations.[21] Reports of erroneous claim denials, long call wait times, and missing patient data that MCOs should have provided to Magellan led the state to delay program implementation for several months before reintroducing it in a phased approach in June 2022.[22] The state has yet to issue public data that would allow evaluation of the program's effectiveness in negotiating supplemental rebates.

2. Expanding Prescription Drug Reporting Requirements

According to the National Academy for State Health Policy (NASHP), 14 states passed drug price transparency laws between 2018 and 2021.[23] These laws typically require one or more entities in the drug supply chain (e.g., drug makers, insurers, PBMs) to provide the state with information on drug prices and/or spending. While there is substantial variation between laws, there are several relatively common features of such legislation.

These laws often require drug makers to notify state agencies of the list price of newly launched drugs or the list price increases they take on existing products. In some cases, manufacturers must only provide data on drugs that exceed certain price thresholds (e.g., the specialty drug price threshold for Medicare, a price increase of more than 10% in a year). Relatively few states require manufacturers to submit net price information, though some ask that manufacturers disclose the aggregate amount of rebates they provide for specific drugs. Several states also require manufacturers to submit information on costs of research and development, acquisition, marketing, production, and distribution. Some states require insurers and/or PBMs to submit information on cost and utilization and, in some cases, the impact of prescription drug spending on per member, per month insurance premiums.

These laws typically include confidentiality provisions that prohibit disclosure of certain data, such as net prices for specific drugs and other information considered by drug makers to be trade secrets. This prohibition is to guard against legal challenges such as that pursued by the Pharmaceutical Research and Manufacturers of America (PhRMA) against the state of Nevada. Nevada enacted a law that would have required manufacturers of essential diabetes medications to provide the state with information on pricing methodology and accounting information that would then be released to the public. PhRMA argued the law violated federal trade secret protections. It is unknown whether courts would have decided in PhRMA's favor, as the case was dismissed after Nevada revised the law to allow manufacturers to request that certain information be kept confidential.[24] States that publicly release information on drug price increases typically do so by providing data in aggregated form that cannot be used to determine specific net pricing information on any single drug.

State policymakers have pursued drug price transparency for two broad purposes. First, transparency requirements can be used to pinpoint sources of apparent pricing dysfunction throughout the many steps in the complex drug supply chain. Policymakers can then use this information to inform future policy that is more precisely targeted to address rising drug prices. Second, transparency around drug price increases may create public pressure that discourages excessive increases.

California policymakers introduced new prescription drug reporting requirements in 2017.[25] Under the 2017 law, drug makers must notify the Department of Health Care Access and Information (HCAI) before they launch a new drug that will be priced at "specialty drug" levels ($830 for a 30-day supply in 2023).[26,27] Drug makers must also provide 60 days advanced notice of a price hike of more than 16% on a drug that costs more than $40 for 30-day supply or shorter full course of therapy. Price increases meeting this threshold must also be justified by describing the specific factors used to determine the size of the price increase. HCAI then posts this information to its website.

California also included prescription drug reporting requirements for health insurers in the 2017 law. All insurers must report to the Division of Insurance (DOI) and Division of Managed Health Care (DMHC) an annual list of the 25 most frequently prescribed drugs, 25 drugs with the highest annual expenditures on a list price basis, and the 25 drugs whose spending increases contribute the most to the year-over-year growth in total annual plan spending. The DOI and DMHC publish this information in aggregate form (contributions from individual payers are not identifiable) in an annual report and on their website. The information is intended to provide policymakers and the public with insight into the impact of prescription drug spending on health insurance premiums.

Determining Net Prices and Sources of Increased Expenditures

California's current prescription drug reporting authority could be enhanced to answer two key policy-relevant questions. First, to what degree is the increase in spending on a list price basis matched by the increase in spending on a net price basis after rebates? And second, to what degree is increased spending for a drug due to higher prices versus higher utilization? Answering these two questions requires volume data along with pricing, fee, and rebate information across different supply chain entities, including drug manufacturers and PBMs. Alternatively, payers can provide pricing and volume information, but those data would not include the fees and discounts paid to other parts of the drug supply chain and so would not provide as transparent a view of the entire system.

The National Academy for State Health Policy (NASHP) has promulgated an approach that would allow state agencies to determine the net price of a drug to different payer types (commercial, Medicaid, Medicare). The model law requires drug makers, PBMs, wholesalers, and insurers to submit information on price, volume, and rebates and includes appropriate protections to ensure the confidentiality of trade secrets.[28]

To ease the administrative burden on drug makers and to ensure clarity regarding which information will be held in confidence, agencies can implement a standard form with data entry fields that are clearly marked to indicate whether a response will be made public or kept confidential. There are already two publicly available standard data request forms that state agencies can draw from as examples. The first, from NASHP, focuses on volume and pricing data

but not clinical evidence.[29] The second form was developed by the Massachusetts Health Policy Commission (HPC) with input from drug makers.[30] The HPC form requires drug makers to report net prices to different payers over the previous five years as well as changes to list price over the same time period. The form also asks drug makers to provide research and development costs and net prices offered to 10 other countries, all of which use CER to inform price negotiations. Finally, the form requires manufacturers to summarize clinical trials and other evidence that describes the drug's efficacy, effectiveness, and other outcomes.

Comparing Net Prices for Existing and New-to-Market Drugs to Prices Determined by Comparative Cost-Effectiveness Analysis

California policymakers could also consider expanding existing drug price reporting requirements to include comparison of net prices to cost-effective price ranges determined by published and/or otherwise publicly available CER. Price comparison could be required for high-expenditure drugs and for newer drugs expected to have high anticipated net prices. These price comparisons are common in both approaches to drug affordability review discussed in the next chapter, but are not generally a feature of transparency laws. Adding CER price comparisons to transparency requirements can allow policymakers and the public to understand the savings that could be achieved if net prices were in line with those suggested by CER.

Further Discouraging Excessive Price Increases

Two approaches to further discouraging excessive price increases in the pharmaceutical drug market have recently emerged. First, the federal Inflation Reduction Act (IRA) included a provision that requires drug makers of single-source drugs and biologics covered under Medicare Part B (which covers drugs administered by a health care provider and a limited number of outpatient drugs) and the majority of drugs covered under Medicare Part D (which covers outpatient prescription drugs) to pay rebates to the federal government for drug price increases that exceed the general rate of inflation for urban consumers. If average prices increase beyond the rate of inflation, drug makers must pay the difference back to Medicare. The penalty for noncompliance, including paying less than the required rebate amount, is equal to 125% of the correct rebate amount.[31,32]

The primary advantages of the IRA's approach are its simplicity and breadth – any drug with a price increase beyond the rate of inflation is subject to the penalty. However, this simplicity has one important drawback: it does not allow drug makers to increase the price of their drugs beyond the rate of inflation when those increases may be justified by new evidence of improved clinical benefit or fewer harms than previously known. It is important to recognize that allowing drug makers to increase prices under these circumstances may incentivize beneficial post-marketing research,

which may identify additional patient subpopulations who would benefit from a drug and will permit clinicians to develop better guidelines to inform choice of treatments.

Another potential issue with the IRA is that these inflationary rebates, which apply only to Medicare's purchases of drugs, are projected to increase national Medicaid drug spending by approximately $15.7 billion dollars from 2022-2031, according to the Congressional Budget Office (CBO).[33] This is because Medicaid already receives statutory inflationary rebates and the IRA is expected to cause drug makers to take smaller drug price increases than they otherwise would have, thus decreasing the size of the Medicaid's rebates over time. In addition, the CBO expects drug makers to increase their launch prices to mitigate the impact of lower price increases over time, and that these cost increases will only be partially offset by Medicaid's rebates off list price (described in Section 1).[34]

This loss of rebate revenue to Medicaid is expected to outweigh any savings the program receives from reduced prescription drug price increases.[35] However, as part of the American Rescue Plan, Congress removed a cap that prevented Medicaid from receiving rebates greater than the average manufacturer price offered for a drug. Once this update takes effect in 2024, Medicaid programs will receive greater rebates from manufacturers who take large price increases; CBO predicts that this will result in $17.3 billion in overall savings for the program, $8.4 billion of which would accrue to states. This may offset the some of the increased spending from the inflationary rebate provisions in the IRA.[36]

ICER has developed an alternative approach to identifying excessive price increases, which is applied in its annual "Unsupported Price Increase" (UPI) reports.[37] For each report, ICER uses commercially available data on average net price for drugs across all payers to develop a list of the top 10-15 drugs whose net price increases in the past year have caused the greatest overall increases in expenditures. ICER then performs CER assessment on clinical studies from the preceding three years to determine whether there is any new research demonstrating greater clinical benefits and/or reduced harms that could justify increasing the price of each drug. Drug makers are encouraged to submit additional information to justify their price increases. Following this process, ICER classifies drugs as having price increases either supported or unsupported by new evidence. With the additional information on net prices described above, a UPI report could generate public pressure and serve as the basis for inflationary rebate penalties.

NASHP has developed an approach that enables states to leverage ICER's UPI reports to collect revenue commensurate to these "unsupported drug price increases."[38] Under the NASHP model, manufacturers who take unsupported price increases must pay the state a penalty equal to 80% of the difference between the revenue from sales of the drug in the state and the revenue that would have been generated if the price increase had been kept to the rate of inflation for urban consumers. These penalties apply only to manufacturers with more than $250,000 in total sales in the state. Manufacturers who do not pay the penalty are fined the greater of an additional 10% or

$50,000 and must provide the state with six months' notification and pay a fine of $500,000 if they want to remove a drug from sale in the state to avoid the penalty. One legal risk of any penalty provision is whether the size of the penalty will run afoul of the Takings Clause of the US Constitution (see discussion of legal considerations in Appendix B for more details).

One unintended consequence of penalizing price increases may be to incentivize even higher launch prices for new drugs to compensate for future lost revenue on existing drugs. Indeed, the CBO projects that the IRA will cause drug makers to do so.[39] To address this concern in lieu of further federal action, state policymakers could consider adding measures that would target drug launch prices, as discussed in sections below.

3. Establishing State-Based Drug Affordability Review Authority

One of the most powerful ways state policymakers have begun leveraging CER is to embed it within prescription drug affordability review authority. To date, this authority has been implemented in two forms: 1) authorizing Medicaid programs to pursue supplemental rebates via an affordability review process; and 2) creating a *de novo* prescription drug affordability board (PDAB) with the authority to set an upper payment limit (UPL) that state (and possibly private) purchasers will pay for a prescription drug. Each approach empowers a state to determine whether the costs of individual drugs are reasonable and, if not, to achieve pricing concessions to improve affordability for payers and patients. California could consider implementing one or both of these approaches as part of its efforts to align prescription drug spending with value.

New York and Massachusetts have implemented versions of the Medicaid-focused affordability approach, while six other states (Colorado, New Hampshire, Maryland, Maine, Oregon, and Washington) are implementing some form of a PDAB. In the sections below we present details on how these programs were created and structured to achieve their goals.

Medicaid Drug Affordability Review

Medicaid programs are required by law to maintain a drug utilization review (DUR) program that monitors whether drugs are being used appropriately. DURs monitor prospective and retrospective utilization patterns to screen for fraud, underuse or overuse, and to ensure drugs are being used in appropriate clinical situations, including considerations of drug-drug interactions, contraindications, and incorrect dosages or durations of treatment. DUR programs are required by law to have a Board of outside experts composed of, at minimum, one-third physicians and one-third pharmacists, with other members having expertise in one or more of the following areas: clinically appropriate prescribing, dispensing, monitoring, use, evaluation, intervention, and quality assurance. New York further empowers its DUR Board to negotiate supplemental rebates for certain prescription drugs. Massachusetts enables a different agency, the HPC, to investigate the pricing and value of high-cost drugs referred to it by the state's Medicaid program, MassHealth, if MassHealth is unable to negotiate a satisfactory supplemental rebate agreement.

As discussed earlier, California DHCS manages the state Medicaid program's contract drug list (CDL). In most cases, manufacturers must agree to provide a supplemental rebate for their product to be included on the CDL; drugs excluded from the CDL require prior authorization.[12] DHCS considers published evidence and stakeholder input on clinical effectiveness, safety, harms, need, potential for misuse, and cost when determining which drugs should be included on the CDL, including

evidence produced by CER. Prior to the implementation of the Medi-Cal Rx program, managed care organizations could implement more restrictive coverage policies and negotiate their own supplemental rebates.[6]

New York

In 2017, New York established a Medicaid drug spending cap which can be used to identify specific drugs for which to seek supplemental rebates.[40] The cap limits overall drug spending growth to the 10-year rolling average of medical inflation (CPI-M) and, when the budget director for the Department of Health (DOH) projects drug spending to exceed that amount, authorizes the DOH to seek supplemental rebates on drugs with the greatest contribution to piercing the spending cap. In its current iteration, the program targets drugs for which total spending or cost per claim, both net of all rebates, is in the top 3% of spending for all drugs.

Once the state identifies the drugs that meet these criteria, it reaches out to the drug makers in an initial attempt to reach a supplemental rebate agreement. Drug makers who agree to provide a sufficient rebate then exit the process. The remaining drugs are referred to the DUR Board, which is authorized to hold a public meeting at which it identifies a target rebate amount through discussion of CER evidence on clinical effectiveness and cost-effectiveness produced by third parties, along with information on R&D spending and other investments (e.g., costs of manufacturing, distribution, marketing, etc.).[41]

The actual target price/supplemental rebate is held in confidence, but once identified it becomes the subject of further negotiation between staff within New York Medicaid and drug makers. New York Medicaid is not permitted to exclude drugs from its formulary if negotiations fail, which ensures that patient access will be unaffected. The negotiating leverage gained through this program is largely driven by the drug maker's desire to avoid the negative publicity from being the focus of a public meeting on inappropriate prices. In addition, if a suitable supplemental rebate is not reached through negotiation, New York Medicaid may apply prior authorization criteria or accelerate collection of rebates to the extent permissible under law. If drug spending is still projected to exceed the growth cap after negotiations conclude for all drugs in the initial list, the state may seek supplemental rebates for other drugs.[42]

According to New York DOH staff, from fiscal years 2017-2022, 140 drugs have been included in the initial list of drugs that contribute to piercing the spending cap. The vast majority of the time the state and drug makers have held successful initial negotiations for supplemental rebates, obviating the need to proceed to a public meeting. According to a leader at New York's DOH, the state's Medicaid program has saved more than $600 million under the drug spending cap authority to date.

Initial negotiations failed for three drugs during this time period, leading to their referral to the DUR Board for public review: Orkambi for cystic fibrosis; Remicade, an immune-modulating drug for several inflammatory conditions; and Spinraza for spinal muscular atrophy. For Orkambi and Spinraza, the DUR Board specified its target price was anchored on comparative cost-effectiveness findings. Although the specific results of the ensuing further negotiations are held in confidence, the state has publicly acknowledged receiving a supplemental rebate from the maker of Orkambi.

Massachusetts

In 2019, Massachusetts authorized the state's Medicaid Program, MassHealth, to negotiate supplemental rebates for drugs. Under this law, if initial negotiations between MassHealth and a drug maker are unsuccessful, MassHealth may refer a drug to the Health Policy Commission (HPC), an independent state agency with an appointed expert governing Board that has authority to oversee health care cost, quality, and access issues. The HPC is empowered to assess whether the drug's price is reasonable.[4,43,44] Drug makers are required to submit a dossier with information regarding R&D costs, pricing for different federal payers and international markets, and CER data produced by third parties on the drug's relative effectiveness versus other alternatives.[30] The HPC also solicits comment from relevant stakeholders including patients, clinical experts, and payers, all of whom may provide information for the Commission to consider during its pricing review. Most of the granular information from this submission is not made public, but the HPC may release the drug maker's narrative summary of the factors used in choosing the drug's list price and price increases, as well as other summary information that does not expose trade secrets.

In addition to the information submitted by the drug maker and by public stakeholders, the HPC is also authorized to consider clinical effectiveness and cost effectiveness analyses from CER and may engage third-party organizations to conduct this research. Similar to the New York approach, the HPC may also hold a public hearing regarding the drug's pricing. The HPC may then post to its website the name of the drug maker and drug reviewed, its assessment of the value of the drug, and its determination of whether the drug maker's pricing is reasonable relative to the drug's value. Throughout this process, the drug maker may continue its negotiations with MassHealth and the drug can be withdrawn from the HPC process if a satisfactory supplemental rebate agreement is reached.

Although this program was enacted in 2019, the HPC has not yet received a referral of a drug from MassHealth of a single drug. It may be that, as in New York, drug makers wish to avoid public scrutiny about whether their pricing decisions exceed reasonable levels. As of November 1, 2021, MassHealth has reported annual cost savings of $171 million from supplemental rebate negotiations and the agency notes that the potential for a public process, even though one has not yet occurred, has had an impact.[45]

Key Strengths and Limitations

Medicaid programs' authority to negotiate supplemental rebates is well established under current law. Although New York's enhanced authority has been in place and active since 2017, it has not been subject to any legal challenges from the pharmaceutical industry. These programs also have the benefit of leveraging existing committee infrastructure within Medicaid (or outside Medicaid in the case of the Massachusetts HPC). With these two key strengths, Medicaid drug affordability review programs have important advantages over alternatives.

However, there are important limitations as well. Perhaps the most notable limitation of this approach is that savings only impact Medicaid spending. While these savings are important, greater overall savings could be achieved under the PDAB approach discussed below, which is able to extend application of fair pricing standards to other state insurance programs (e.g., state employee insurance) and, potentially, commercial insurance programs as well.

Another limitation is that, to date, Medicaid drug affordability review programs have not universally tried to address launch prices of new, very expensive drugs. New York's approach targets only those drugs with sufficient cost and utilization to cause affordability challenges, while the law in Massachusetts allows targeting of existing drugs with more than $10 million in annual spending or any drug with a list prices greater than $25,000 per year, including new drugs.[4] If policymakers consider expanding the scope of price negotiations to include new drugs, Medicaid drug affordability review programs could develop criteria describing which new drugs should enter the supplemental rebate negotiation process. One potential approach would be to set thresholds based on the potential budget impact of a new drug, calculated by multiplying its launch price with the eligible patient population; another would be to follow Massachusetts' example by establishing a price threshold.

Elements of Success

In interviews, staff at the New York and Massachusetts agencies tasked with negotiating supplemental rebates suggested several best practices to ensure successful implementation of a Medicaid drug affordability review program.

First, any agency tasked with negotiating supplemental rebates should seek to reach agreements for portfolios of drugs whenever possible. At baseline, this approach can achieve greater savings through fewer individual negotiations. In addition, this prevents drug makers from negotiating a supplemental rebate for a targeted drug, then attempting to shift market share toward a comparable product that has not been subject to the affordability review process (e.g., a shift from a once-daily formulation to a twice-weekly extended-release product). Drug makers may be willing to enter into portfolio agreements to maintain or increase market share for several of their products in a given therapeutic area.[45]

Second, agencies should be ready to consider outcomes-based contracts as part of achieving lower overall costs for expensive single-use and short-term therapies such as gene therapies. In many cases, these treatments promise transformative or curative benefits and command multi-million-dollar prices. Despite their high price tags, they often fare well in CER because they provide substantial clinical benefits for patients and frequently offset the need for other treatments and/or supportive care, the cost of which can be substantial through many years. In an interview, a leader at the New York DOH noted that drug makers have been more willing to assume a large portion of risk because they are confident their product provides superior outcomes to existing therapies. While, from the state's perspective, this means that Medicaid agencies may end up paying close to the asking price for these products for most patients, these therapies represent a good use of limited funds because of how drastically they obviate the need for other care; in addition, the state would pay substantially less than the list price for the proportion of patients who do not benefit from these therapies.

Third, agencies should ensure that several Board members have experience with the conduct and/or interpretation of CER and, more specifically, health economics outcomes research, the component of CER that pertains to cost-effectiveness analysis. CER is a highly complex field and has only recently gained increased influence in a US context. As such, many health care professionals may lack sufficient familiarity to correctly interpret the results of cost-effectiveness analysis. Board members with such expertise can serve as a resource for other members whose expertise is primarily in clinical or pharmacy practice.

Finally, interviewees recommended that any Medicaid affordability review process include multiple "off-ramps" where drug makers can agree to provide supplemental rebates without going through full public review. This structure communicates good faith on behalf of the state and encourages drug makers to provide supplemental rebates to avoid the time and costs associated with compliance.

Prescription Drug Affordability Boards

Several states are in various stage establishing PDABs, many of which set in-state UPLs for prescription drugs. The UPLs are not technically binding; a drug maker can decide whether to accept the reduced payment or may withdraw a product from sale in the state. This approach was developed by NASHP after several efforts were struck down by courts (see Appendix B for a discussion of legal issues).[46,47] In this section, we summarize the updated approach and compare key aspects of the currently established PDABs in Tables 2.1 through 2.3.

Under the most recent NASHP model, a board of outside experts is recruited to review evidence on a drug's price (including list and net price), market competition, the price of the drug in other states and countries, the impact of price on patient access and health equity, and the drug's cost-effectiveness, which inherently involves analysis of clinical outcomes. The PDAB is then authorized

to establish UPLs using the aforementioned information for all payments for the drug by payers in the state; ERISA plans are exempt but may opt in to the UPL. In this way, the PDAB is intended to minimize the risk of patent preemption challenges by setting the maximum allowable *payment* for a drug, rather than setting its *price* (see Appendix B for additional details). The overall approach is modeled after the manner in which states regulate the cost of public utilities – by evaluating the operating costs of the provider and rejecting proposed rates that are deemed to be excessive, effectively capping the amount that can be paid for those services, while still ensuring utility providers remain profitable.[48]

Under the NASHP model, PDAB's may not consider measures of benefit that assign "a reduced value to the life extension provided by a treatment based on the pre-existing disability or chronic health condition of the individuals whom the treatment would benefit." This language effectively bans the use of a metric called the "quality-adjusted life year" (QALY), a measure that researchers use to study the effects a drug has on length and quality of life for patient populations, for any life-extending drug. QALYs are expressed as a number between 0, representing death, and 1, representing a year in perfect health. In cost-effectiveness research, a common outcome is the amount of money that must be spent to gain one QALY. Some patient groups, particularly those representing patients with chronic and/or disabling conditions, object to the use of cost per QALY gained measures because a treatment that provides incremental benefits to a severely ill population may not be found to warrant a high price versus a treatment that provides a benefit of similar magnitude for a patient population that is less sick to begin with. This is because a QALY is calculated by multiplying length of life by quality of life.

The NASHP model, while prohibiting the QALY, does permit the use of cost-effectiveness with other measures of health gain, such as a related measure called the "equal value of life years gained" (evLYG) or cost consequence outcomes such as cost per hospitalization avoided. The evLYG assigns the same high level of quality of life to any life extension provided by a treatment. In other words, all life-extending effects of treatment are assigned the same value regardless of initial disability or the severity of the condition, while still allowing researchers to compare the effects of different treatment options on patient quality of life in the period before life extension.

Enacted Prescription Drug Affordability Boards in Six States

Tables 2.1 through 2.3 below compare key aspects of the NASHP model and the six established PDABs. Of these six PDABs, two (Colorado and Washington) may set UPLS without requiring additional approval from state government, although those set by the Colorado board may be overridden by a majority of the House Joint Health Insurance Committee or the Senate Health and Human Services Committee. The Maryland PDAB must submit a UPL action plan for approval from the state's Legislative Policy Committee or the governor and attorney general before it is able to set UPLs for specific drugs. The other three PDABs (Maine, New Hampshire, and Oregon) may not set

UPLs; Maine's PDAB may instead work with individual insurers in the state to identify other ways to achieve cost savings such as seeking supplemental rebates, moving to a common formulary for all public insurers, bulk purchasing, etc.

UPLs set by the Colorado PDAB apply to all in-state purchasers and payers, and the Board may set 12 UPLs per year from 2022 through 2024; there is no limit for subsequent years. If its UPL action plan is approved, the UPLs set by Maryland's PDAB will initially only apply to state and local government purchasers and payers, including Medicaid, and the board is tasked with developing a recommendation about whether the payment limits should be expanded to commercial payers. While Washington's PDAB may set UPLs that apply to all purchasers and payers in the state (public and commercial), there are several provisions that make doing so challenging. Washington's PDAB may not set a UPL prior to 2027 and, after that, can only set 12 each year. Washington's PDAB is only authorized to consider drugs that have been marketed for 7 or more years, though policymakers are currently considering removing this limitation.[49]

The following tables compare other key aspects of the NASHP model and enacted PDABs, including details of how much a drug must cost to be eligible for negotiation and details of which metrics the PDAB may consider.

Table 2.1. Comparison of Upper Payment Limit (UPL) Authority Across NASHP Model and Enacted PDABs

PDAB Authority	NASHP Model[47]	Colorado[50]	Maryland[51]	Maine[52]	New Hampshire[53]	Oregon[54]	Washington[55]
Ability to set UPLs?	Yes	Yes. UPL can be overridden by majority vote of House Joint Health and Insurance Committee or Senate Health and Human Services Committee	UPL authority implemented through a "UPL Action Plan" that must be approved by the Legislative Policy Committee or the Governor and Attorney General	No	No	No	Yes
Limit to Number of UPLs per year?	None	12 per year for first 3 years, then no limit	None	N/A	N/A	N/A; study limitation of 9 drugs and 1 insulin product per year	12 per year, none can be set until 2027. 24 affordability reviews can be performed each year
Entities Subject to UPLs	All purchasers and payers. ERISA plans may opt into UPLs.	All purchasers and payers; self-funded plans may opt in to UPLs. Individuals who purchase a drug for use by themselves or a family member are exempted. Purchases/reimbursements required by state/federal law are exempted.	State and local government purchasers and payers (including health benefit plans on behalf of state/local government), and drugs purchased for or paid by the MD Medicaid program Law requires PDAB to study/recommend whether UPLs should be extended to all purchasers and payers in state by December 1, 2023.	N/A	N/A	N/A	All purchasers, health carriers, and all Health Exchange plans. Employer-sponsored self-funded plans may opt in. Carriers may disregard UPL if the drug is deemed medically necessary for a patient.

PDAB Authority	NASHP Model[47]	Colorado[50]	Maryland[51]	Maine[52]	New Hampshire[53]	Oregon[54]	Washington[55]
Other UPL Provisions	None	Individuals may request exemption from a UPL if a drug maker removes drug from sale in state. An independent commission will adjudicate requests.	Exempts drugs that are on the FDA prescription shortage list. UPLs may be re-evaluated if there is a shortage of the drug in MD.	Instead of UPLs, board identifies cost growth targets and may work with public payers to identify other methods to achieve cost savings, including supplemental rebates, common formulary for all public payors, prohibit formulary inclusion, formulary placement changes, bulk purchasing, etc.	Same "other" provisions as in Maine	None	UPLs (and other new rules) cannot be implemented until 90 days after the start of the next legislative section.
Enforcement Mechanisms	Drug makers who seek to withdraw drug from sale in state must file 6 months days' advanced notice or pay $500k fine	Drug makers who seek to withdraw drug from sale in CO must file 180 days' advanced notice or pay $500k fine	Not specified	N/A	Fines of up to $1k per day (up to $25k total) for violating any provisions of law	N/A	$100k fine for drug maker noncompliance. Drug makers who withdraw drug from sale in state are prohibited from re-entry for 3 years unless they agree to UPL.

Table 2.2. Comparison of Targeted Drugs Across NASHP Model and Enacted PDABs

PDAB Authority	NASHP Model[47]	Colorado[50]	Maryland[51]	Maine[52]	New Hampshire[53]	Oregon[54]	Washington[55]
Able to Target Launch Prices?	Yes	Yes	Yes	Yes	Yes	Yes	No. Eligible drugs must have been marketed for ≥ 7 years
Brand Drug Targets	List price ≥ $3k	Launch list price ≥ $30k per year or course of treatment	Launch list price ≥ $30k per year or course of treatment	25 most frequently prescribed drugs, 25 costliest drugs by total spending; 25 drugs with highest cost increases by total state spending. Can also review public payer spending.	Drugs with list price that would place them on Medicare Part D specialty tier	Drug makers: list price ≥$100 for a one-month supply or shorter full course of treatment, drugs with prices that exceed Medicare Part D price threshold for specialty drugs. Payers: 25 most frequently prescribed drugs, 25 most costly drugs by total annual spending, 25 drugs that caused greatest increase in total plan spending Other: insulin products marketed in state	List price ≥$60k per year or course of treatment
Generic Drug Targets	Same as brand targets	List price ≥ $100 per 30-day supply, <30-day full course of treatment, or unit	List price ≥ $100 per 30-day supply, <30-day full course of treatment, or unit	Same as brand drug targets	Not specified	Same as brand drug targets	List price ≥ $100 per 30-day supply, <30-day full course of treatment, or unit

PDAB Authority	NASHP Model[47]	Colorado[50]	Maryland[51]	Maine[52]	New Hampshire[53]	Oregon[54]	Washington[55]
Biosimilar Drug Targets	Launch list price not at least 15% lower than reference product	Launch list price not at least 15% lower than reference product	Launch list price not at least 15% lower than reference product	Not specified	Not specified	Not specified	Launch list price not at least 15% lower than reference product
Targets Price Increases?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Brand Drug Price Increase Targets	List price increase of ≥$300 in previous 12 months, WAC increase of ≥200% in previous 12 months	List price increase of ≥10% per year or course of treatment	List price increase of ≥$3k per year or course of treatment	25 drugs with highest year-over-year cost increases by total spending	Increase of >20% per pricing unit	Net increase of ≥10% or more for drugs costing ≥$100 for one month supply or shorter full course of treatment	Price increase of ≥15% in any 12-month period, or 50% cumulative increase over 3 years
Generic Drug Price Increase Targets	Same as brand targets	List price increase of ≥200% over 12-month period	List price increase of ≥200% over 12-month period	Same as brand drug price increase targets	Drugs costing at least $10 with >20% price increase	Same as brand drug price increase targets	List price increase of ≥200% over 12-month period
Other Drug Target Provisions	May consider other drugs referred to PDAB. May consider drugs included in payer reports (top 50 most frequently dispensed, top 50 most costly by total annual spending, top 50 drugs with greatest price increases, top 50 most costly drugs to consumers, drugs with substantial rebates)	None	Any drug that may create affordability challenges for state health care system and patients	None	None	Exempts drugs indicated for rare diseases or conditions	Exempts drugs indicated for rare diseases or conditions.

Table 2.3. Comparison of Allowable Cost-Effectiveness Metrics Across NASHP Model and Enacted PDABs

PDAB Authority	NASHP Model[47]	Colorado[50]	Maryland[51]	Maine[52]	New Hampshire[53]	Oregon[54]	Washington[55]
QALY Provision	None	Bans use of cost per QALY outcomes, but not QALY in isolation	None	None	None	Bans use of QALY and similar measures to identify subpopulations for which drug would be less cost-effective.	Bans use of QALY to identify subpopulations for which drug would be less cost-effective
Provisions for other metrics	Requires all life extending effects of drugs to be valued equally	Prohibits other measures that "discount the value of a life because of an individual's disability or age"	None	None	None	Requires quality of life to be measured equally for all life-extending drugs.	Requires all life extending effects of drugs to be valued equally.

Key Strengths and Limitations

The primary strength of PDABs is that they can be framed more broadly than Medicaid-specific drug affordability review programs, thereby expanding the scope of cost savings for payers and patients within the state. Second, PDABs are new entities that can facilitate engagement with leading health care and health economics experts within the state and beyond.

But these strengths also represent potential risks for PDABs in comparison to Medicaid-specific programs. The broader inclusion of payers means that PDABs present greater risks for legal challenges (see Appendix B for further details). And the fact that PDABs are new entities introduces complex considerations regarding their constitution, leadership, and funding.

There are other important potential limitations for policymakers to consider. Drug makers may be able to evade the UPLs set by PDABs. For example, one option would be to withdraw a product from sale in states that have set UPLs. While this possibility is handled in different ways by enacted PDABs, no approach currently prohibits the practice, as such a provision would likely be struck down by courts. If a UPL is established for a drug in California, some drug makers may decide that, even at reduced prices, the California market is simply too large and lucrative to leave. But others may determine that it is better to forego sales in California to avoid triggering the Medicaid "Best Price" provision, which requires pharmaceutical drug makers to sell their drugs to Medicaid programs at the lowest price they offer to any other purchaser with few exceptions. In interviews, stakeholders mentioned that drugmakers could also continue to offer the drug for sale in the state but refuse transactions at the UPL.

There may also be challenges in extending the UPLs set by a PDAB to state Medicaid program. This would most likely occur if the PDAB set a UPL that was lower than the price reached through mandatory rebates.[56] Because Medicaid is required to cover all drugs, it would not be able to comply with the UPL. This vulnerability could be addressed by enabling Medicaid to negotiate supplemental rebates with the aid of CER, or by exempting Medicaid programs from the UPL.

Elements of Success

The ability to review the full suite of evidence produced by CER is essential to any PDAB's effectiveness. The comprehensive comparative clinical effectiveness review is essential to the board's ability to understand the relative benefits and disadvantages of different treatment options to various patient populations. The economic analysis, in turn, provides the PDAB with an objective measure of whether a drug's price is reasonable and suggests the range of prices that would be appropriate given current clinical evidence. More specifically, the PDAB should be allowed to review CER that uses aggregate measures such as the evLYG to allow the board to make equitable judgments across disease areas. Otherwise, the PDAB will essentially be tasked with determining whether the money spent for a desired clinical outcome in one disease area is reasonable

compared to the money spent to achieve some other clinical outcome in another disease (e.g., cost per stroke averted vs. heart attack avoided, severe asthma attack prevented, etc.); there is no established methodology to guide this sort of comparison. Furthermore, without CER's economic analyses, PDABs must determine how to establish a reasonable price by weighing disparate pieces of clinical and economic evidence; another task for which there is no established methodology and, as a result, could increase the risk of legal challenge due to the fundamentally arbitrary nature of such an approach.

The ability to set UPLs is another crucial element of success, according to one PDAB leader. Without this authority, PDABs function solely as a research and reporting organization, which PDAB employees argued would have minimal, if any, impact on drug prices. The NASHP model allows PDABs to develop the methods to assign UPLs through rulemaking. Maryland's PDAB follows a more conservative approach, as it is required to propose its methods for setting UPLs to the legislature for approval, after which they can be applied to any targeted drugs. In contrast, requirements that each UPL be authorized by an outside entity would slow (and possibly prevent) the PDAB from implementing payment limits and would also expose the process to potentially inappropriate influence from special interest groups. This could lead to a system where more powerful interest groups are able to avoid UPLs being applied to treatments for certain diseases.

PDAB employees also highlighted the importance of including a funding mechanism as part of authorizing legislation, to ensure that the board is able to immediately begin its work, rather than needing to identify a funding source beforehand. And finally, policymakers may wish to consider how best to appropriately insulate the work from the influence of well-funded special interest groups (e.g., drug makers, payers, and, in some cases, advocacy organizations).

Safeguard language for the use of cost-effectiveness metrics

As noted above, some patient groups, especially those representing disability and rare disease communities, have voiced concerns that cost-effectiveness analysis can be used as a tool to deny needed care.[57] The core of this concern is their belief that metrics for the quality of life, such as the QALY, undervalue treatments that impact populations with severe, chronic conditions.

The evLYG offers an important methodological option to avoid the perception of discrimination in the way the QALY assigns value to extended lifetime. As part of the broader effort to address concerns in this area, ICER has also developed language to safeguard against potentially discriminatory applications of cost-effectiveness analysis.[5] Different versions of this language have been used in several enacted PDABs and other state policies that seeks to leverage cost-effectiveness analysis to manage drug spending:

> *In considering cost-effectiveness, [THE STATE] cannot use cost-effectiveness analyses that use the cost-per-quality adjusted life year or similar measure to identify subpopulations for which a treatment would be less cost-effective due to severity of illness, age, or pre-existing disability. In addition, for any prescription drug that extends life, [THE STATE'S] analysis of cost-effectiveness must not employ a measure or metric which assigns a reduced value to the life extension provided by a treatment based on a pre-existing disability or chronic health condition of the individuals whom the treatment would benefit.*

While this language may not be strictly necessary for a Medicaid-focused approach, as the program is legally required to cover most drugs and thus could not refuse coverage based on unfavorable cost-effectiveness findings, it may help reassure patients that their goal is to ensure fair pricing rather than the denial of care. This language should be viewed as an important inclusion for PDABs to prevent the misuse of cost-effectiveness research because other payers are not subject to the same coverage requirements as Medicaid departments.

4. Expanding the Use of CER to Negotiate Drug Prices and Support Value-Based Benefit Designs

Evidence generated by CER can aid the efforts of pharmacy and therapeutics (P&T) committees in managed care plans, which determine the clinical circumstances under which an insurer will cover a drug. Public and commercial payers can use economic analyses performed as part of CER to suggest a range within which pricing can be considered reasonably aligned with the benefit to patients. In its reports, ICER calls these price ranges "health benefit price benchmarks," while they are also colloquially called "value-based price benchmarks." These benchmarks are frequently used in negotiation between payers and drug makers, to inform formulary tiering, and to implement novel benefit designs that reward patients for choosing drugs that are priced fairly.

Using CER to Negotiate Drug Prices

As discussed in earlier sections, cost-effectiveness analyses conducted as part of CER can provide an objective guide to one of the key questions that underpin price negotiations: "what is a fair price?" There are numerous ways this information can be used to support more active negotiation in seeking lower costs aligned with patient benefit. First, publicly available price benchmarks can be used by commercial and public payers to seek lower list prices and/or net prices. Public statements and confidential anecdotes from many private payers describe negotiations in which the active use of publicly available CER price benchmarks gave payers an objective, specific target, as well as forcing drug makers to have persuasive arguments for higher prices. This experience over many years shows that independently conducted CER can serve to level the playing field during drug price negotiations, as drug makers often conduct their own economic analyses that are likely to present results that are more favorable. Using cost-effectiveness results to spearhead more aggressive negotiation has also been a hallmark of the Veteran's Health Administration (VHA), which has reported achieving substantial cost savings without adverse effects on patient access to drugs.[58]

Even outside of a formal Medicaid drug affordability review program, CER price benchmarks can be used by Medicaid and health exchange plans to seek lower prices. In California, the recent implementation of the Medi-Cal Rx program, which shifted the state's Medicaid prescription drug purchasing away from individual managed care plans to a statewide fee-for-service model, presents policymakers with greater scale to apply CER price benchmarks in negotiation.

Key Strengths and Limitations

The major strength of applying CER to price negotiation is that it gives payers a more specific, independent, and publicly available price benchmark that can increase their confidence and ability

to press for more reasonable pricing. The limitations to payer leverage in price negotiations, however, are not solved just by having a more specific price point, even one that can create headlines for how much lower it is than the price announced by drug makers.[59] Payers cannot walk away from the table and decide not to cover important new drugs that have no close analogue in clinical effectiveness, and therefore all the pressure they can bring to the negotiation may not be enough to get drug makers to restrain their pricing on the basis of CER findings.

Another barrier to the use of CER to guide price negotiations is the inherent misalignment that rebates can create for payers to seek the largest rebate, even if that means the plan sponsor is not paying the lowest net price.[7] Greater transparency into those rebate and fee arrangements, with more rebates fully passing through to plan sponsors, might alleviate some of the problem, but rebates have proven a stubborn issue to solve, whether through legislative or business model approaches.

Using CER to Support Value-based Benefit Designs

There are several ways in which CER is currently and could further be utilized to support value-based benefit design in California. Below, we highlight several options that public and/or commercial insurers can use to ensure their plan offerings align with the best available clinical evidence, and provide good value for money.

Formulary Tiering

CER can support linkages between price negotiation and formulary tiering, but it can also be used solely to determine which tier of the formulary a drug is placed on at whatever price is being charged. Payers can create such "value-based formularies" that place all drugs priced at or below a health benefit price benchmark at more favorable tiers, while moving treatments priced above that range to high/specialty tiers. This approach rewards patients with lower out-of-pocket costs for choosing high-value treatments while discouraging them from choosing low-value alternatives. This approach has been taken most notably by Premera Health Plan in the Pacific Northwest, which launched a value-based formulary in 2010. Using cost-effectiveness results to determine the tiering of key drugs, this formulary was shown to reduce overall drug expenditures by a significant $10 per member per month (PMPM) while maintaining utilization levels and appropriate use of essential drugs for conditions such as diabetes and asthma.[60]

"Pay-up-to" Formulary Design

Price benchmarks determined through CER could be applied in concept to create a formulary benefit design that limits plan sponsor payment rates to a fair market ceiling price. The basic idea behind a pay-up-to formulary design is that when drug makers charge prices beyond a fair price ceiling as determined by CER, the plan sponsor will only pay up to the fair price. The payer

administering the benefit could create incentives for drug makers to reduce prices to this ceiling price, perhaps by placing the drug on a preferred tier to drive higher volume. A "pay up to" approach would ideally incentivize drug makers, especially of drugs in competitive classes such as auto-immune drugs, to reduce their prices to levels that will minimize patients' exposure to high out pocket costs, as they are likely to lose market share versus competitors whose drugs are less costly to patients.

The idea of a pay-up-to formulary design builds off the similar approach many plan sponsors have adopted of a "reference-priced" formulary, in which drugs that are judged to have equivalent clinical effectiveness are reference-priced to the lowest cost option, often a generic. The pay-up-to formulary extends this idea to all drugs, even those that are clinically superior to other options, placing a ceiling reimbursement price tied to how well the drug works (with higher ceiling prices for more effective drugs), which will usually be lower than what will be charged by the drug maker.

Although enticing conceptually, there are important barriers to implementing this formulary design idea, and no formal pilot test has yet occurred in the US market. Plan sponsors are unenthusiastic about approaches that may only load more financial burden onto individual patients, especially if they truly have no other effective treatment option. And payers balk at the conflict between this benefit design and their standard designs centered on capturing the highest rebates. Nonetheless, plan sponsors, particularly employers who have sufficient expertise or consultant help to negotiate with their payer, may wish to ask their payer to present them with an option for a pay-up-to approach in at least one condition area.

This approach is not suitable, however, for Medi-Cal, which is subject to legal requirements that set low patient out-of-pocket costs, or for plans offered through the health exchange, which must provide benefits that meet specific standards for actuarial value that vary based on the metal tier of the plan: bronze, silver, gold, and platinum.

Exclusionary Formularies

Pay-up-to formulary designs are, in a way, the antithesis of a current benefit design whose use is continuing to expand: exclusionary formularies. Exclusionary formularies exclude a growing number of drugs that a payer determines are not "needed" by patients given other available alternatives.[61] Clinical CER is used to help support the clinical equivalence of drugs in order to justify the exclusion of other, more expensive (or lower-rebate) alternatives. But a variation on this approach could be designed to apply the cost-effectiveness results from CER to determine which drugs are excluded. This would follow a general approach taken in countries such as the UK, where a formal cost-effectiveness range largely determines whether a drug is covered by the National Health Service.

CVS Health began offering an exclusionary formulary in 2018 for self-funded clients of its Caremark business line that was the first in the US to make formal reference to cost-effectiveness thresholds as a basis for formulary exclusion.[62] CVS Health only considers exclusion on the basis of cost-effectiveness for drugs that have therapeutic alternatives, and in practice has never announced a single exclusion on this basis, but has claimed to have received lower net prices in several examples from drug makers seeking to ensure that they were not at risk of exclusion.

Although applying cost-effectiveness to expand the list of drugs excluded from the formulary is relatively simple to implement, it has significant drawbacks, including the natural reaction of patients and clinicians that excluding drugs smacks of rationing. Concerns about the potential discriminatory elements of QALYs within cost-effectiveness rise to the fore.[57] In addition, the actual potential for cost-savings has not been evaluated. Policymakers should be very cautious in considering any approach of this nature, and we believe the pay-up-to formulary, despite its own risks and limitations, offers a better alternative for applying CER in support of novel benefit designs.

Waste-Free Formularies

The Purchaser Business Group on Health (PBGH), in collaboration with Integrity Pharmaceutical Advisors, has developed the concept of "waste-free formularies."[63] Under this approach, employers seek to reduce spending on several categories of drugs that are considered wasteful: "me-too" drugs that add little clinical value compared to other available treatments, combination drugs for which the individual drugs are available at lower cost, prescription drugs with over-the-counter alternatives, and brand drugs with generic alternatives. Employers and the payers who administer this approach can ensure that it is robust and evidence-based by using CER to identify spending on drugs for which more cost-effective alternatives are available and clinically appropriate.

The primary barrier to implementation of an intensive version of the formulary is the added administrative burden on payers and employers, as it would require retrospective review of prescribing data and outreach to prescribers and patients to encourage them to switch to a more cost-effective treatment.

Covered California Could Set Standards for Use of CER

Covered California could request more specific information on how payers use CER to inform benefit and formulary designs during the "request for proposal" (RFP) process. One approach would be to require affirmation and examples demonstrating that P&T committees consider evidence produced by CER when determining which drugs will be included on the formulary, how they should be covered, and to inform tier placement. Covered California could also require plans to demonstrate how they consider cost-effectiveness analyses when negotiating drug prices; this use would need to remain separate from the work of P&T committees, which are prohibited from considering cost.

Key Strengths and Limitations

For value-based benefit designs, the strengths of applying CER in novel ways also arise from the ability CER provides to align patient cost sharing, or plan sponsor maximum reimbursement, or even inclusion on the formulary, with explicit evidence on patient benefit and cost-effectiveness. But here too the existing rebate ecosystem creates barriers to implementing new benefit designs that would interrupt the flow of rebate revenue to various parties in the system. In particular, the PBM business model has proven so durable and profitable that the leading PBMs, benefiting now from unprecedented market share concentration, will find it difficult to ever be the first to adopt a major change that threatens those traditional revenue streams. This barrier exists across public and commercial insurance markets.

Value-based benefit designs that shift patient cost-sharing may also be challenging to implement within the state health exchange. As mentioned earlier, Covered California plans face the unique requirement of meeting specific actuarial value standards. In an interview, a Covered California representative noted that any effort to decrease out-of-pocket costs for one service must be met with an increase in costs for another service to maintain these standards. While this may represent a new administrative challenge, it does not preclude the use of CER. In fact, CER would provide objective evidence that allows health plans to determine which drugs should be placed on lower versus higher formulary tiers.

Federal and state mental health and substance use parity requirements may pose a barrier to the implementation of CER in plan design across commercial and public insurance markets. Broadly, mental health and substance use parity laws require most health plans to provide comparable coverage for mental health and substance use services as they do medical and surgical services, both in terms of quantifiable treatment limits (e.g., quantity and duration limits, type and level of cost-sharing, etc.) and non-quantifiable treatment limits (e.g., P&T processes, prior authorization policies, step therapy, etc.). Health plans are permitted to provide more generous coverage of mental health/substance use services as compared to medical/surgical health services, but not the other way around.[64]

In practice, this means that health plans would need to ensure that their use of CER does not result in higher patient out-of-pocket costs for mental health as compared to medical services. For example, if a plan decided to place generic maintenance medications for a chronic medical condition at the $0 copay level in a value-based benefit design, they must also place generic maintenance medications for chronic mental health conditions at the same level.

Plans must also ensure that their P&T committees apply the same processes with the same degree of stringency across physical and mental health services. Parity laws have always required health plans to apply the same processes across the medical/mental health divide. More recently, a 2021 update to federal mental health parity laws now requires health plans to perform comparative

analyses regarding their application of non-quantifiable treatment limits, including demonstrating what evidence and standards they apply across medical and mental health services.[65] Plans should be prepared to demonstrate that their use of CER complies with legal requirements.

Several stakeholders noted variation in how different states interpret and enforce mental health parity laws and suggested that California is generally considered to be among the stricter states. There is room, however, for the Department of Health Care Services to issue affirmative guidance on the appropriate use of CER in plan and benefit design. CER involves a rigorous comparison of the clinical and economic evidence for various treatment options and, applied equally, poses no challenges to the goal of achieving mental health parity. Indeed, the consistent use and application of evidence promotes the ability to justify when coverage is appropriate and, conversely, when limitations may be appropriate. In other words, CER provides a way to establish and demonstrate mental health parity.

5. Conclusion

CER produces information that can guide multiple approaches to assuring that patients have access to the drugs that are appropriate for their clinical situation at an affordable price commensurate with clinical benefit. Unfortunately, drug prices are often far higher than those suggested by fair price benchmarks produced by cost-effectiveness analysis, one branch of CER, and yet our current drug market, with greater pricing leverage left in the hands of drug makers than in any other country, and with payers and plan sponsors mesmerized by rebate revenue, has failed to make the best use of both branches of CER to reduce costs and assure optimal access. California policymakers have a history of leading the nation in tackling complex social problems, and CER offers them new avenues for seeking progress in drug pricing and access.

While no single action will be sufficient to address the rising cost of prescription drugs, states have begun implementing several approaches that, in concert, are likely to produce meaningful savings for states and individuals. The experience of these states, as well as that of other public and commercial payers, have demonstrated that expanded applications of CER can enhance the effectiveness of transparency legislation, affordability review authority, and enable novel value-based approaches to formulary and benefit design. State policymakers and purchasers in California are uniquely positioned to consider a number of steps to further integrate CER into insurance benefit design, formulary development, and price negotiation to drive progress in achieving a health care system that can guarantee fair pricing, fair access, and future innovation.

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Appendix A. List of Interviewed Organizations

- America's Health Insurance Plans (AHIP)
- Blue Shield of California
- California Department of Health Care Services
- California Department of Health and Human Services
- CalPERS
- Colorado Prescription Drug Affordability Board
- Covered California
- Department of Health Care Access and Information (HCAI)
- Massachusetts Health Policy Commission (HPC)
- Maryland Prescription Drug Affordability Board
- National Academy for State Health Policy (NASHP)
- New York Department of Health (Drug Utilization Review Board)
- Purchaser's Business Group on Health (PBGH)
- UC, Davis School of Law
- The Source on Healthcare Price and Competition at UC College of Law, San Francisco

Appendix B. Legal Considerations

Dormant Commerce Clause

Congress is empowered to regulate interstate commerce by the Commerce Clause of the Constitution. The US Supreme Court has interpreted the clause to prohibit states from passing legislation that would unduly burden interstate commerce, even if Congress has not passed a law pertaining to a specific interstate commerce issue. This interpretation is called the "Dormant Commerce Clause," (DCC) with "dormant" referring to the lack of Congressional action.[66]

According to NASHP, laws targeting prescription drugs are vulnerable to DCC challenges if they impose costs that are disproportionate to the expected public benefit or regulate activity that takes place in other states (e.g., requiring that drug prices in one state be no higher than the prices in another state).[48]

The DCC has posed a barrier to many state legislative efforts to lower drug spending, in part because the pharmaceutical supply chain almost invariably includes transactions that cross state lines (e.g., drug makers sell their products to wholesalers who then sell products to pharmacies; each entity may be in a different state). For example, the US Court of Appeals for the Fourth Circuit struck down a Maryland law (HB 631) that would have recouped money spent on "unconscionable" drug price increases – price hikes not justified by increased production costs or efforts to expand access to drugs for which patients have no "meaningful choice" or have little competition. The circuit court's rationale relied on the finding that no drug makers or wholesalers reside in Maryland and, as a result, the law impermissibly regulated commerce outside of the state's borders by setting a price.[67] Some observers believe this case was wrongly decided based on a misunderstanding of the pharmaceutical supply chain (i.e., drug makers already manage systems to charge different prices to various entities across the country, so the Maryland law created no real burden) and a misapplication of the tests to determine DCC violations and argue that states should not view the decision as foreclosing similar efforts.[68] Nevertheless, NASHP developed rate setting model legislation, discussed in Section 2, that should avoid the concerns raised by the circuit court. States can also stipulate that any affordability legislation is targeted at drugs that are actually sold in the state, as opposed to drugs that are made available for sale, to ensure that the law cannot be interpreted as applying to out-of-state transactions.[56]

Patent Preemption

The federal government issues patents, which provide for exclusive marketing rights for an invention in exchange for public disclosure of that invention. The patent system is designed to reward and encourage innovation through these exclusive rights while facilitating other innovations through disclosure of the patent.[69] Patent preemption refers to the ability of the federal

government to preclude or curtail state activities that may impinge upon the exclusive rights of patent holders. This can occur when Congress explicitly prohibits state authority (express preemption), when Congressional regulations are so pervasive that there is no reasonable room for state activity (field preemption), or when state regulation conflicts with federal rules, in which case the federal rules take precedence (conflict preemption).[70]

The pharmaceutical industry may raise concerns that any state-based to regulate their pricing power impinges on the rights granted to them by the federal patent system. A NASHP-commissioned legal analysis by Robin Feldman et al.[70] finds this argument deficient for several reasons. Feldman et al. argue that there can be no express preemption because federal patent law relating to drugs does not prohibit state regulation of prices. Field preemption is also unlikely because the patent system solely grants an entity the right to exclusively market a product; it does not guarantee any level of profitability. Conflict preemption is similarly unlikely to be a factor because federal patent law does not regulate price. In addition, states already regulate many products and services that have numerous patent protections; for example, public utility commissions regularly determine acceptable rates for electricity providers even though their product undoubtedly involves multiple patents.[70]

Nevertheless, Feldman et al. argue that best practices require that any effort to regulate drug prices (or, as is the case in the NASHP PDAB model legislation, payments) apply equally to both branded and generic products so as not to alter the balance of patent-based incentives to develop new drugs.

Regulatory Takings

The Constitution's Fifth Amendment protects property owners from government seizure of private property without just compensation; this is referred to as the "Takings Clause." This typically refers to physical property, but the concept has also been extended to circumstances where government regulations are so severe as to effectively represent such seizures.[70]

As it pertains to drug pricing regulations, the Takings Clause ostensibly prohibits state or federal government from implementing a law that would confiscate all the revenue from drug sales. However, Feldman et al. note that the Supreme Court has permitted the government to seize private land at a 90% discount and argue that a drug pricing regulation would pass muster so long as it allows the drug maker to make some level of profit on the sale of their drug.[70] In terms of drug price increase legislation, the risk of legal challenges increases as the tax penalty nears 100%, so legislators may wish to set a lower penalty. However, higher penalties are expected to be a more effective deterrent against excessive price hikes.[71]