

Regulatory Barriers Impair Alignment of Biopharmaceutical Price and Value





Executive Summary

Paying for prescription medicines based on their value to patients is increasingly seen as a promising technique to combat rising medication costs. Value-based arrangements work by linking the price of a prescription medicine to its effectiveness, and by the manufacturer and the payer agreeing to share risk. For example, a biopharmaceutical manufacturer might receive one price for a medication that produces the desired and anticipated outcome, but refund a portion of the price of the medicine and cover associated costs, such as hospitalizations, for a medicine that fails to do so.


While other parts of the health care sector are moving quickly toward value-based arrangements, adoption has been slow for biopharmaceuticals due to difficulty agreeing on measurable outcomes, lack of required infrastructure and regulatory barriers.

In a new study conducted by the National Pharmaceutical Council, leaders in the payer and biopharmaceutical industries identified four regulatory barriers that are standing in the way of value-based contracts in health care. In an effort to more fully understand these regulatory limitations, we quantified the impact of removing them. Participants pointed to the inability to contract outside of the Food and Drug Administration (FDA) label, Medicaid's "best price" rules, Medicare's Average Sales Price (ASP) and the Anti-Kickback Statute (AKS) as the major regulatory barriers to advancing value-based agreements. Both payers and manufacturers regarded the inability to contract outside of the FDA label to be the greatest barrier to value-based contracting implementation.

Key Findings


Barrier #1: Inability to Contract Outside of the FDA Label

Currently, prescription medicine pricing cannot be based on an outcome, such as hospitalizations, if that outcome was not examined in the clinical trials included in the FDA-approved label. This is problematic because the outcomes in the FDA label often are not appropriate measures on which to build a risk-sharing agreement because they are not measurable or clinically relevant. Also, the link between the value-based agreement and the payer's budget (the financial risk) may not be clear.

 **How we could address this barrier:** Allow value-based arrangements to consider outcomes outside of the FDA label.

Barrier #2: Medicaid Best Price Rules Cap Medicaid Rebates

Medicaid's best price rules limit the rebates that manufacturers can provide for medications covered under Medicaid. Medicaid's best price is set quarterly based on the single lowest price available from the manufacturer to any entity, such as payers and providers, in the U.S. The regulations stipulate that a manufacturer must provide Medicaid either the maximum rebate in the market or a 23.1 percent rebate, whichever is higher. Medicaid's best price rules, therefore, increase the cost of contracting, creating a financial incentive to limit rebates on applicable medications.

 **How we could address this barrier:** Create a carve-out so that Medicaid's best price caps do not apply to value-based contracts.


Barrier #3: ASP Precludes Pricing for Distinct Medication Indications

Under the FDA approval process, most medicines have a single brand, although each medication may treat multiple conditions and provide greater value for one condition over another. ASP does not take into consideration the value associated with multiple indications. That poses a significant barrier to value-based contracting for physician-administered medications, as it creates the potential for a physician to experience financial loss under a buy-and-bill approach.

 **How we could address this barrier:** Remove ASP as a barrier to indication-based contracting to align medication value with net price.

Barrier #4: AKS Inhibits Useful Patient Tools

The federal AKS effectively prohibits manufacturers from utilizing risk management tools that could bolster patient outcomes and save money in federal health care programs. Manufacturers in value-based arrangements take on the risk for successful outcomes. For example, if a medication does not work for a patient, the manufacturer loses money, even if the failure is due to factors out of the manufacturer's control. Manufacturers could institute programs aimed at giving the patient the best chance of successful treatment, including patient education, nurse coaching, case management support, benefit assistance, adverse event monitoring and outcomes monitoring. The current AKS, though, threatens large penalties for providing anything of value that could be seen as driving business toward a manufacturer.

 **How we could address this barrier:** Provide an anti-kickback safe harbor for value-based contracts.

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Background

In response to rising costs, the health care sector is moving quickly toward value-based cost management strategies. There have been numerous examples of this evolution for providers with increased use of value-based reimbursement methods (e.g., accountable care organizations). In comparison, adoption of value-based payment approaches has been slow for biopharmaceuticals, with flat or utilization-based rebates remaining the standard.

Value-based arrangements can enable payers to reduce the risk of exposure to failed outcomes and make prescription medicines more affordable for patients. However, adoption has been slow due to difficulty agreeing on measurable outcomes, lack of required infrastructure and regulatory barriers. The federal government's willingness to consider reducing regulations creates an opportunity to accelerate movement toward value-based reimbursement for pharmaceuticals. In an effort to more fully understand these regulatory limitations, we identify the most important regulatory barriers and illustrate how they are problematic.

Regulations Inhibit Value Alignment with Price

To better understand the slow uptake of value-based contracting for medicines, we conducted in-depth interviews with 12 key stakeholders among manufacturers and payers. The individuals interviewed included a senior vice president at a pharmacy benefit manager, a vice president of contracting at a national managed care organization (MCO), a chief medical officer at a regional MCO, a chief pharmacy officer of an integrated delivery network, a medical director of an

integrated delivery network, a former Medicaid actuary director and six vice presidents of pricing and contracting from different pharmaceutical manufacturers. We asked each participant to prioritize the regulatory barriers that presented the greatest challenge to value-based pricing.

The participants identified four regulatory barriers that inhibit both payers and biopharmaceutical manufacturers from engaging in value-based agreements, including the inability to contract outside of the Food and Drug Administration (FDA) label, Medicaid's "best price" rules, Medicare's Average Sales Price (ASP) and the Anti-Kickback Statute (AKS). Both payers and manufacturers regarded the inability to contract outside of the FDA label to be the greatest barrier to value-based contracting implementation.

Using the information derived through the stakeholder interviews, we designed three hypothetical case studies and modeled the quantitative impact of removing the regulatory barriers related to contracting outside of FDA labeling, Medicaid's best price rules and Medicare's ASP. We then assessed the policy implications of the current AKS and identified potential opportunities for clarification, revision and reform.

Barrier #1: Inability to Contract Outside of the FDA Label

Currently, value-based agreements cannot be based on an outcome, such as hospitalizations, if that outcome was not examined in the clinical trials included in the FDA-approved label. This translates into higher overall costs to the health care system, and is problematic because the outcomes included in the FDA label often do not provide the most appropriate or measurable outcome on which a payer and manufacturer can base a risk-sharing agreement. Also, the link to the payer's budget, and therefore the financial risk, may not be clear.

The idea behind value-based arrangements is for the payer (the insurer covering the medicine) and the manufacturer to share financial risk. Under current rules, the payer generally assumes the full risk, paying for the medication regardless of how well it works. Using a commercially available medication as a prototype, we developed a hypothetical example to show how the removal of this barrier, and the ability to structure value-based contracts using outcomes outside the FDA label, could provide savings to the health care system.

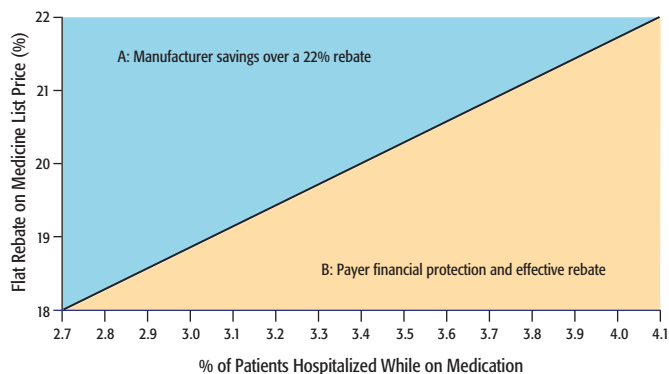
We built our case example using the following criteria: (1) the medicine’s performance was gauged by an outcome readily measured with claims data, (2) the outcome could be directly linked to payer budget impact and (3) the outcome was not included in the FDA-approved label. In addition, in our case example, Phase III clinical trials for the medication did not examine impact on hospitalizations, but post-market clinical trials concluded that the medicine reduced hospitalizations. In this hypothetical case example, a payer requested a flat 22 percent rebate to cover its financial risk and account for the underlying clinical risk associated with a new therapy, but the manufacturer was unwilling to provide such a discount. Instead, the two parties negotiated a two-year value-based agreement that shifted some of the financial risk to the manufacturer. In this scenario, the hypothetical two-year contract was based on numbers of hospitalizations, an outcome that was not included in the therapy’s FDA label.

Under the hypothetical agreement, the manufacturer agreed to provide full reimbursement for the cost of the medicine and related hospitalizations for all patients that exceeded the agreed-upon number of total plan hospitalizations. If the payer’s hospitalization rate was consistent with the rate of the post-market clinical trial, then the rebate was 18 percent. If the hospitalization rate exceeded that of the post-market clinical trial, the manufacturer was required to pay \$27,000 in rebates for each additional hospitalization, which was equal to the cost of the medication and hospitalization.

For the payer, the contract created value by eliminating exposure to failed outcomes. For example, the payer received

a 20 percent rebate when the hospitalization rate was equal to the midpoint between the rate of hospitalizations of the post-market clinical trial and the rate of hospitalizations seen outside the trial. A hospitalization rate equal to that seen outside the clinical trial produced a 22 percent rebate. Area B in Figure 1 demonstrates financial protection to the payer.

Figure 1: Potential Savings and Financial Protection When Using a Risk-based Contract Outside of the FDA Label



Savings to the manufacturer would start at 4 percentage points (an 18% rebate), as long as efficacy was consistent with clinical trials, but savings would decline as the hospitalization rate increased. The 4 percentage point savings reflect the value created as the cost of access is lowered. Area A in Figure 1 shows the potential savings to the manufacturer resulting from this contract, as compared to a flat 22 percent rebate agreement.



How we could address this barrier:

Allow value-based arrangements to consider outcomes outside of the FDA label.

This example highlights how a tangible outcome that is not included in the FDA label can be a source of value creation for both the payer and the manufacturer. In the long run, value-based contracting has the potential to help reduce growing health costs as failed outcomes are a source of waste.



HOW WE CALCULATED

The hypothetical value-based contract used the following details:

- It offered an 18 percent flat rebate for a hospitalization rate consistent with the rate of the post-market clinical trial.
- For each hospitalization in excess of the number occurring in the post-market clinical trial, the manufacturer reimbursed the full cost of the medicine, effectively providing a 100 percent rebate.
- There was a two-year medication cost of about \$10,000 per patient when there was 100 percent compliance.
- There were one million covered lives for the hypothetical commercial insurance plan.
- There was a two-year cost of \$18,849 per patient requiring hospitalization. This cost was assumed to cover any reoccurring hospital costs over that period.

Medication costs were based on the December 2016 wholesale acquisition cost (WAC), which is the manufacturer's reported list price for wholesalers. Medication adherence was assumed to be 100 percent.

We calculated the rebate for the value-based arrangement by identifying the number of hospitalizations in excess of those seen in the post-market clinical trial, then multiplying that number by the sum of medicine and hospitalization costs.

Next, we divided that number by medication costs and added it to the 18 percent starting point. Rebates were calculated for a range of hospitalization rates and compared against a base rebate of 20 percent to determine the impact to both the payer and manufacturer.

Barrier #2: Medicaid Best Price Rules Cap Medicaid Rebates

Medicaid’s best price rules stipulate that manufacturers must provide certain rebates for medications covered under Medicaid. Medicaid’s best price is set quarterly based on the single lowest price available from the manufacturer to any entity, such as payers and providers, in the U.S. (excluding 340B Drug Pricing Program providers, bona fide service fees, Medicare Part D and limited mail-order pharmaceutical benefit managers). The regulations stipulate that a manufacturer must provide Medicaid either the maximum rebate in the market or a 23.1 percent rebate, whichever is higher. This example highlights how Medicaid’s best price rules currently increase the cost of contracting, thereby creating a financial incentive to limit rebates on applicable medications.

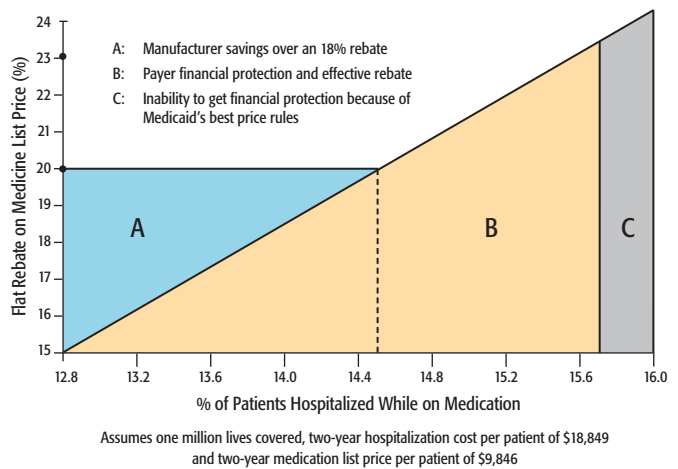
To demonstrate the cost impact of Medicaid’s best price rules, we created a hypothetical value-based agreement for a hypothetical product and plan. This value-based agreement between the payer and manufacturer included a 15 percent flat rebate, which was adjusted upward based on the number of hospitalizations relative to those seen in the clinical trial (the primary indication for the blinded product).

In this case example, we measured the impact of Medicaid’s best price rules on this agreement by calculating the full contract cost, which is the sum of the rebate determined by the agreement with the plan plus the additional Medicaid costs resulting from Medicaid’s best price rules. We then converted the full contract cost to an effective rebate, which reflected the total cost in terms of a per-unit rebate to the plan. One key difference from the prior example is that the product used in this example has an impact on hospitalizations as its primary indication.

For illustration purposes, let us assume that the manufacturer did not cap the rebate and the plan experienced a 16 percent hospitalization rate. Per the value agreement, this would result in a 23.9 percent rebate to the plan. Due to Medicaid’s best price rules, this contract would add 0.8 percent to the rebate

on all Medicaid sales for this product, which is equal to an additional \$16 million per year in costs for the manufacturer. On a per-unit basis, Medicaid’s best price rules result in the effective rebate to the plan rising from 23.9 percent to 27.1 percent when total costs are considered. This 3.2 percentage point increase represents the financial incentive for the manufacturer to cap the rebate at 23.1 percent.

Figure 2: Potential Savings, Financial Protection and Medicaid’s Best Price Limitations When Using a Risk-based Contract



What are the consequences for the payer should the manufacturer cap the costs? If the manufacturer caps the rebate at 23.1 percent, the payer would lose \$29,000 of financial protection for every patient with a hospitalization that results in a rebate above this 23.1 percent threshold.



How we could address this barrier:

Create a carve-out so that Medicaid’s best price caps do not apply to value-based contracts.

The payer and manufacturer industries have both called for a carve-out for value-based contracting in Medicaid’s best price rules. Such reform would have to be defined in a way to prevent non-value-based agreements from being included. In addition, the long-term financial impact to Medicaid would need to be understood.



HOW WE CALCULATED

The product used in this example measured hospitalization levels as an indication of success of the hypothetical treatment. Medication costs were based on the most current WAC prices (December 2016), and hospitalization-related costs were the same as in the previous case. Hospitalizations were analyzed between the clinical trial and post-market surveillance rates to determine the likelihood of the rebate exceeding 23.1 percent.

In this scenario, the payer and manufacturer agreed to a value-based contract with the following details:

- **It offered a 15 percent flat rebate.**
- **For each hospitalization in excess of the number occurring in the clinical trial, the manufacturer reimbursed the full cost of the medicine, effectively providing a 100 percent rebate.**
- **For each patient with hospitalizations in excess of the number occurring in the clinical trial, the manufacturer paid 100 percent of hospitalization costs.**

In order to calculate the effective rebate that included additional Medicaid costs, we needed to know the percent of sales from both the plan and Medicaid. Our scenario assumed that Medicaid comprised 20 percent of medication sales and that the insurance plans comprised 5 percent of medication sales.

The additional cost for Medicaid was calculated by first subtracting 23.1 percent from the contract rebate and then multiplying the difference by the annual sales to Medicaid. This resulted in the total annual cost impact.

The conversion of the total cost impact to a unit's effective rebate involved the following steps:

- 1. The additional costs from Medicaid needed to be prorated to account for differences in sales volume; otherwise, the unit rebate difference would be understated. The first step was to calculate the ratio of Medicaid sales to plan sales. In our example, four units of medication were sold to Medicaid for every unit sold to the hypothetical plan (e.g., a ratio of 5 percent to 20 percent). This is important because it implied that every additional dollar per medication unit paid to Medicaid as a result of this contract could be viewed as an additional \$4-per-unit cost to this value contract.**
- 2. The resulting incremental Medicaid per-unit rebate increase was calculated using the following formula:
$$(\text{plan rebate} - 23.1 \text{ percent}) * \text{ratio of Medicaid sales to plan sales}$$**
- 3. The effective plan rebate was calculated by adding the plan rebate per the contract and the resulting incremental per-unit rebate increase to Medicaid.**

Barrier #3: ASP Precludes Pricing for Distinct Medication Indications

Many medicines have multiple indications, meaning they treat more than one condition. For example, TNF inhibitors treat many conditions, including rheumatoid arthritis, Crohn’s disease and ulcerative colitis. The potential value of TNF inhibitor treatment is different for each of these conditions. However, under the current FDA approval process, the majority of medications have a single brand, which means that there is one list price for that medicine by dose for all treated conditions; the same price is paid regardless of use. Indication-based pricing is a rebate-based structure whereby the payment for a medication is determined by the value associated with the condition for which it is used. Under this arrangement, differences between the price paid and the value associated with the condition in which it is used are refunded to the payer via a rebate.

There are challenges to indication-based pricing whether the medicine is administered through a pharmacy or by a physician. When the medication is dispensed through the pharmacy, the primary challenge is Medicaid’s best price rules, as described in the prior example.

When a medicine is administered in a doctor’s office, the physician purchases the medication and then is reimbursed by the payer after administering the medication. This is called a

buy-and-bill system. Both Medicare and a large percentage of commercial insurance plans use Medicare’s ASP, the volume-weighted average of price paid net of rebate, to determine that reimbursement.

This case examines how ASP acts as a barrier to indication-based pricing when medications are reimbursed under a buy-and-bill system. In this scenario, we selected an oncology medicine with three FDA-approved indications that used buy-and-bill reimbursement. The selected agent had varying levels of relative benefit versus the standard of care (SOC) and SOC prices, which allowed us to demonstrate how indication-based pricing may be applied.

Table 1 illustrates why there is a need for indication-based pricing from the payer perspective. The first column highlights how utilization was distributed across the three indications. We calculated the value-based price for each indication based on the SOC. The value-based price of the medicine was \$20,000 per month for the first indication, \$8,000 per month for the second indication and \$9,000 per month for the third indication. Broken down by indication, comparing ASP-based reimbursement with the value-based price revealed that the payer saved \$9,700 for Indication 1, while overpaying by \$2,300 for Indication 2 and \$1,300 for Indication 3. This equates to overpaying \$1,000 per treated month per member. For a plan with one million members, the impact of the current approach would be an additional \$4.5 million per year in additional costs.

Table 1. Impact of ASP Reimbursement on Payers

Disease	Total Utilization Percentage	SOC Price Per Month	Efficacy benefit vs. SOC (OS)	Value-based Price	ASP + 3% Reimbursement	Payer Savings Per Month	Average Payer Cost Per Month
Indication 1	10%	\$10,000	+10 months	\$20,000	\$10,300	\$9,700	(\$1,000)
Indication 2	80%	\$6,000	+2 months	\$8,000		(\$2,300)	
Indication 3	10%	\$7,000	+2 months	\$9,000		(\$1,300)	

Legend: ASP: Average Sales Price, SOC: Standard of Care, OS: Overall Survival

Let us now assume that an indication-based contract is put in place across all payers so that the net price paid (i.e., including rebates) would be equal to the value-based prices listed in Table 1. Table 2 illustrates the impact this indication-based agreement would have on the physician under an ASP-based reimbursement. This indication-based arrangement would lower the ASP for this medication by \$700 in six months, from \$10,000 to \$9,300. Assuming that the medication acquisition costs remained flat, the physician would lose \$421 per month per patient for this product when reimbursed on an ASP basis, and would lose \$50,520 per year for treating 10 patients each month.



How we could address this barrier:

Remove ASP as a barrier to indication-based contracting to align medication value with net price.

Removing ASP as a barrier to indication-based contracting provides the opportunity to align medication value with net price, which has the potential to lower costs to the health care system and provide additional access to more effective medicines for patients. An indication-based contracting carve-out for ASP would have to be defined in a way to prevent non-value-based contracts from being included. Furthermore, the long-term financial impact to Medicare would need to be understood.

Table 2. Impact of ASP Reimbursement on Physicians 6 Months After New Contracting

Disease	Total Utilization Percentage	Value-based Price	ASP	ASP + 3% Reimbursement	Physician Medicine Acquisition Costs	Average Physician Cost Per Month
Indication 1	10%	\$20,000	\$9,300	\$9,579	\$10,000	(\$421)
Indication 2	80%	\$8,000				
Indication 3	10%	\$9,000				

Legend: ASP: Average Sales Price



HOW WE CALCULATED

We calculated a monthly cost for the medication's SOC, as indicated in clinical treatment guidelines for first-line treatment by disease state. To calculate the value-based indication price, we assumed an additional monthly cost of \$1,000 for each additional month of survival beyond the SOC. For example, a five-month survival improvement would add \$5,000 to the monthly cost. The results of these calculations are shown in Table 1. Utilization mix was estimated based on the epidemiology of selected diseases and utilization characteristics of the product.

To determine how much payers overpaid or underpaid for the medicine based on each indication, we took the difference between the ASP + 3 percent reimbursement cost and the value-based price. The overall impact to the payer was calculated by taking a weighted average of these differences. The annual budget impact to a plan with one million lives was calculated by multiplying this weighted average by the total prevalence for all three conditions among one million lives.

Next, we examined the implications of value-based contracting by indication on physician reimbursement. To model this impact, we assumed that the average of all manufacturer discounts was equal to the value-based prices we calculated. We calculated the new ASP by taking a weighted average of the three value prices calculated for the blinded product. This new ASP lagged the contract rebate by six months, but, once established, remained in place as long as the average discounts remained unchanged. Physician

ASP + 3 percent reimbursement was calculated using the new ASP value. We conservatively assumed that the physician medication acquisition cost was equal to the original ASP (\$10,000). The impact to the physician was calculated by taking the difference between the medicine acquisition cost and the new reimbursement rate. The annual impact was estimated based on a practice that treated 10 patients per month.

It is important to note that the above examples do not take into account implementation costs, including monitoring health outcomes, utilization and other metrics that may negate the cost benefits of the arrangement. In addition, we made no attempt to calculate national savings, as the benefits would vary based on the terms of the agreements and the underlying populations.

Barrier #4: AKS Inhibits Useful Patient Tools

The federal AKS is a criminal statute that prohibits the exchange of, or the offer to exchange, anything of value in an effort to induce or reward the referral of federal health care program business. Because there is uncertainty as to how this statute aligns with value-based purchasing agreements, many manufacturers refrain from offering such agreements.

In order for manufacturers to accept additional risk, they need to be able to use the appropriate tools (e.g., patient adherence programs) to manage this risk. However, manufacturers often do not develop or offer such programs due to the perceived risk of violating the federal AKS. During qualitative interviews, one payer described a situation in which he was offered a suite of value-added services to accompany a manufacturer's portfolio of products for a chronic, high-budget disease. During negotiations, the payer requested that a second manufacturer, which also had a portfolio of medications within this same disease, offer similar services. This manufacturer's legal team, however, believed this request to be in violation of AKS, and the payer was forced to make formulary decisions without equivalent offerings.

The current regulation provides penalties large enough to inhibit manufacturers from engaging in anything that could be seen to fall under this statute. Examples of programs or activities that could be viewed as violating the AKS include patient education, nurse coaches, case management support, benefit assistance, adverse event monitoring and outcomes monitoring. These programs have benefits beyond value-based contracts, including improved intermediate outcomes that may increase long-term patient outcomes. Additionally, manufacturer programs may also decrease administrative burden for providers.



How we could address this barrier:

Provide an anti-kickback safe harbor for value-based contracts.

Creating safe harbor policies would allow for the programs necessary to enable more value-based contracts, and additional clarification of the AKS would benefit patients, providers, payers and manufacturers.

Conclusion

Value-based contracting provides an opportunity to improve economic efficiency and address rising medication costs. Our analysis shows how current regulations prevent these contracts from reaching their full potential. We illustrated how current regulations that prevent the use of outcomes outside the FDA label eliminate an important risk-sharing opportunity. Next, we demonstrated how Medicaid's best price rules create an artificial and inefficient cap on potential risk sharing between payers and manufacturers. The final quantitative example showed how ASP makes indication-based contracting difficult for physician-administered medicines. All of these regulatory barriers could be removed with policy changes, but that would not be sufficient without accompanying changes to the AKS. In order for manufacturers to accept more risk and create additional efficiencies for the health system, clarification on safe harbors under the AKS needs to be established to allow manufacturer use of appropriate risk management tools, such as patient adherence programs.

Value-based contracting is not a panacea for rising medication costs, as these contracts have their own limitations, including infrastructure costs, additional administrative costs and data challenges. They are also limited to those medicines with readily measurable outcomes. However, they are an important tool to match price with value that is not being used to its full potential.



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