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Reforming Reimbursement for the US Food and Drug Administration's Accelerated Approval Program to Support State Medicaid Programs

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Reforming Reimbursement for the US Food and Drug Administration's Accelerated Approval Program to Support State Medicaid Programs

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Abstract

IMPORTANCE The US Food and Drug Administration (FDA) has an accelerated approval program that has become the subject of scholarly attention and criticism, not only for the FDA's oversight of the program but also for its implications for payers.

OBSERVATIONS State Medicaid programs' legal obligations to provide reimbursement for accelerated approval products have created fiscal challenges for Medicaid that have been exacerbated by industry's changing use of the accelerated approval program over time. Although strategies for accelerated approval reforms have been proposed, most focus on reforming the FDA's accelerated approval pathway and product regulation without taking into account the implications of this pathway for state Medicaid programs. There is a need for policy reforms that balance the goal of speeding approval of important medicines with states' real concerns regarding spending on medications with little evidence of clinical benefits. Areas of potential reform include formulary exclusion, Medicaid rebates, value-based pricing, and consolidated purchasing or carve outs.

CONCLUSIONS AND RELEVANCE Policy makers may wish to consider options for reforming reimbursement for accelerated approval products in addition to reforms to the FDA's operation of the pathway. Policy reform proposals can provide a range of options to evaluate trade-offs of access and pricing.

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Introduction

The US Food and Drug Administration (FDA) has an accelerated approval program that has recently become the subject of considerable attention and criticism. The accelerated approval program permits the FDA to approve products that have shown improvements on surrogate (rather than clinical) end points, but once marketed, manufacturers face no constraints on their ability to set prices for these medications. Less attention has been paid to the association between accelerated approval and insurance coverage for these drugs. If accelerated approval drugs have yet to show evidence of clinical benefits, payers may wish to limit their coverage—particularly given the lack of pricing constraints—until such evidence is found.

Different payers have different legal tools available to limit coverage of expensive prescription drugs, including those approved through the accelerated approval pathway. Private payers often have the authority to exclude drugs from coverage, and many have used this authority after the FDA's controversial 2021 decision to approve the Alzheimer disease drug aducanumab (Aduhelm) using this pathway.[1] Medicare has the authority to limit coverage for drugs that are not reasonable and necessary, a rarely used power it applied regarding aducanumab due to the lack of reported clinical benefits when weighed against the potential for harm.[2] But state Medicaid programs lack these authorities and are generally legally required to cover essentially all FDA-approved drugs, including accelerated approval products, despite their lack of supporting clinical evidence.[3]

Although policy makers and experts have begun to propose various strategies for potential accelerated approval reforms,[4,5] most focus on reforming the FDA's processes for approving and regulating these products. Previous work regarding the financial implications of the accelerated approval pathway for state Medicaid programs[6,7] provides context regarding the need for coverage and reimbursement reforms for drugs with accelerated approval status. Herein, we provide a more comprehensive examination of the legal obligations of payers to provide reimbursement for products approved via the accelerated approval pathway, particularly through state Medicaid programs, explain how industry's changing use of the accelerated approval program has exacerbated fiscal challenges for Medicaid, and propose and analyze novel policy reforms that would balance the goal of speeding approval of important medicines with states' concerns regarding spending on medications with little evidence of clinical benefits.

The Accelerated Approval Program

The accelerated approval program was created in 1992, during the HIV/AIDS crisis, with the goal of expediting the approval of certain drugs for serious or life-threatening conditions. Rather than wait for clinical trials to show beneficial treatment effects on clinical end points, the program permits the FDA to approve products showing improvements on surrogate end points that are reasonably likely to be associated with clinical benefits.[8] However, manufacturers are typically required to conduct confirmatory postapproval clinical trials to support those clinical benefits. The FDA may remove a product from the market if the manufacturer does not conduct the required confirmatory trials or if those trials fail to show the expected clinical benefits.[8]

Changes Over Time

The accelerated approval program has evolved substantially since its establishment. A previous study[6] found that, in the pathway's first decade, only 40 approvals were granted for HIV/AIDS medications (40%), oncologic products (30%), and other conditions (30%). Since then, the program has changed in 2 key ways. First, the frequency of program approvals has increased. Between 1992 and 2010, there was a mean of 4.6 approvals per year. Between 2011 and 2020, this number increased to 12.9 approvals per year.[6] Second, the conditions for which manufacturers seek accelerated approval have also changed, shifting toward oncologic products. In 2020, 28 of the 30 approvals made were for products with oncologic indications, most of which were highly focused (eg, treatment must be for refractory illness or after previous specific courses of treatment).[6] Given the program's focus on conditions with unmet medical need and a recent shift toward precision science, this shift toward oncologic indications is perhaps not surprising.

Another study found that on average, sponsors receiving accelerated approval between 2009 and 2016 completed their confirmatory clinical trials and received full approval from the FDA within approximately 3 years.[7] However, some sponsors had not yet completed their confirmatory trials and were beyond the FDA's specified timelines to do so (9 products, or 16% of approvals). These rates of completion varied for oncologic and nononcologic products, with nononcologic products taking far longer to receive full approval (>6 years vs <3 years) and being more likely to have exceeded the FDA's specified timelines (36% of approvals for nononcologic products compared with 11% of approvals for oncologic products).[7]

Program Criticisms

The accelerated approval program has come under increasing criticism for 2 broad reasons. The first relates to the functioning of the program as administered by the FDA. Not only do many accelerated approval products take several years to complete their confirmatory clinical trials, but several products do so beyond the FDA's own specified timelines. For example, when the FDA approved eteplirsen (Exondys 51) for the treatment of Duchenne muscular dystrophy in 2016, the deadline for

completion of confirmatory trials was 2020.[9] Yet the trials are not expected to be complete for several more years.[10]

Furthermore, when manufacturers fail to complete confirmatory studies or when those trials fail to show clinical benefits, the FDA is often slow to request and enforce a drug's removal from the market. Although hydroxyprogesterone caproate (Makena) was approved in 2011 to treat recurrent preterm birth, in 2019 its confirmatory trial failed to demonstrate clinical benefits.[11] The FDA did not formally propose to withdraw the drug until October 2020, but it remains on the market, and the FDA did not hold a hearing on the topic until October 2022.[11] Likely in response to growing criticism, the FDA has recently been increasingly active in proposing product withdrawals. For example, 14 accelerated approvals for cancer indications without confirmed clinical benefits were withdrawn between December 2020 and August 2022, whereas only 7 oncologic indications had been withdrawn before that time.[12]

In addition, confirmatory trials have become the subject of debate. The accelerated approval pathway may require confirmatory trials to demonstrate the expected clinical benefit. However, in the oncologic context, a product's conversion to full approval is frequently based on a surrogate end point (typically progression-free survival) rather than on the clinical benefit of overall survival.[13] The rationale for using surrogate end points for both accelerated and full approval is not often clearly stated.

Another criticism of the program relates to the pricing of accelerated approval products, which is beyond the FDA's purview. The program imposes no limitations on pricing while confirmatory trial results are pending despite the lack of evidence regarding clinical benefits.[14] Although some insurers may be able to limit coverage of some accelerated approval drugs, others—especially Medicaid—cannot.

Medicaid Coverage of Prescription Drugs

Although prescription drug coverage is optional for state Medicaid programs, all states have chosen to cover drugs, recognizing their importance to patient care. A "grand bargain" struck in 1990 required that state Medicaid programs choosing to cover prescription drugs must cover essentially all FDA-approved drugs, with a few statutorily specified exceptions, such as cosmetic products. As a condition of the bargain, state Medicaid programs receive preferred pricing for covered drugs. Specifically, manufacturers must agree to provide large statutory rebates off of the average manufacturer price, insulate Medicaid from price increases outpacing inflation, and offer the best price available to a specified set of payers.[15]

The US Centers for Medicare & Medicaid Services (CMS) has taken the position that state Medicaid programs' requirement to cover essentially all FDA-approved drugs includes accelerated approval drugs.[3] States also have limited ability to use other tools available to commercial payers, such as patient cost sharing, to disfavor products with limited evidence of clinical efficacy. Although states are permitted to negotiate supplemental rebates beyond the statutory requirements, many accelerated approval drugs are intended to treat unmet medical needs and manufacturers of such drugs have few if any competitors, meaning that states may not be successful in these supplemental negotiations. Therefore, state Medicaid programs are constrained in a way that private insurers and Medicare are not. As noted previously, several private insurers and Medicare have limited coverage of aducanumab on the grounds that the drug is not medically necessary. However, Medicaid cannot decline to cover the drug.[16] Thus, state Medicaid programs face unique budgetary pressures from accelerated approval drugs that lack evidence of clinical efficacy. In previous work, we reported that although accelerated approval drugs represented less than 1% of Medicaid drug use, they represented an outsized share (between 6% and 9%) of annual Medicaid drug spending net of rebates between 2015 and 2019.[6]

State Efforts to Address Spending on Accelerated Approval Drugs

Given the quality of evidence available for products at the time of approval and their high prices, several key Medicaid stakeholders have taken steps to exclude or limit payment for some drugs covered under the accelerated approval program. Three state Medicaid programs (Massachusetts, Tennessee, and Oregon) have submitted section 1115 waivers to CMS requesting permission to exclude drugs with limited evidence of clinical benefit, although Tennessee's waiver went beyond accelerated approval products. In 2018, CMS denied Massachusetts's waiver request.[17] In early 2021 CMS granted Tennessee's request as part of its broader block grant waiver, although CMS has since requested the waiver's removal.[18] In 2022, Oregon submitted a waiver request that closely resembled the one from Massachusetts, with the aim of excluding drugs with limited evidence of clinical benefit from coverage,[19] but Oregon later removed this request from its application.[20] The Medicaid and CHIP (Children's Health Insurance Program) Payment and Access Commission (MACPAC) recommended taking another approach, proposing options for increasing the mandatory minimum rebates owed to Medicaid by manufacturers of accelerated approval products tied to the completion of confirmatory clinical trials.[21] These actions reflect growing pressures on Medicaid programs to provide access to products for beneficiaries while working within their real budget constraints.

Reform Strategies to Assist State Medicaid Programs

We examine 4 proposed strategies to assist state Medicaid programs in the challenges they face regarding accelerated approval drugs. These strategies (**Table**) are targeted to the criticisms of the program—incentives to complete confirmatory trials, the use of clinical end points in those trials, and unconstrained pricing practices—in a way that could provide broad benefits to state Medicaid programs. Although these strategies all have the potential to address these criticisms, they vary with respect to the policy tools needed to implement them, their political feasibility, and their operational challenges.

Formulary Exclusion

One reform option would provide state Medicaid programs with authority currently exercised by Medicare and private insurers: the ability to exclude accelerated approval drugs from coverage on the grounds of medical necessity. More specifically, state Medicaid programs could investigate for

Table. Proposed Medicaid Reimbursement Reform Strategies

Strategy	Essential components	Key design decisions
Allow for formulary exclusion	It permits Medicaid to exclude accelerated approval drugs from coverage on an evaluation of the supporting clinical evidence.	The choice to implement this policy at either the state or federal level would create different administrative burdens on different actors.
	It enables Medicaid to act in situations when the FDA may be slow to do so.	The scope of permitted formulary exclusions could jeopardize patients' access to accelerated approval medications that may be clinically beneficial but have not completed confirmatory trials.
	It places Medicaid on a more equal footing with Medicare and private payers with regard to bargaining.	
Medicaid rebate reform	It enables Medicaid to obtain greater rebates for accelerated approval drugs without completed confirmatory trials.	Its efficacy is dependent on the size of the rebates.
	It builds on the existing rebate program, which has been found to be effective in ensuring that Medicaid programs obtain lower prices than many other payers, and CMS already has expertise in administering the program.	Depending on the Medicaid market share for a particular product, manufacturers may be able to mitigate decreased revenue by setting initial prices even higher.
	It may reduce costs while ensuring access for patients.	
Value-based pricing	It allows Medicaid to evaluate the clinical evidence in support of an accelerated approval drug and identify reimbursement rates accordingly, especially while confirmatory trials are pending.	It creates new administrative burdens for Medicaid and would require CMS to develop greater expertise in this area.
	It adopts an approach that has worked effectively in a range of other contexts.	
Consolidated purchasing or carve outs	It would insulate budget-constrained states from the cost of products that have not yet shown clinical benefits.	The federal government would need to choose how to build in additional features to respond to the evidentiary and pricing criticisms of the accelerated approval program.
	It has the ability to reduce states' costs while ensuring access for patients.	

Abbreviations: CMS, US Centers for Medicare & Medicaid Services; FDA, US Food and Drug Administration.

potential exclusion from coverage accelerated approval drugs that have not yet shown clinical efficacy.

There are different ways to implement such a reform proposal. Some ways are feasible with executive action, whereas others require legislative changes. One option would be to permit states to obtain waivers, such as those requested by Massachusetts and Oregon, to exclude these drugs from coverage after evaluating existing evidence. Although CMS has cast doubt on whether these waivers are permissible by rejecting the waiver request from Massachusetts,[17] both the applying states and legal scholars have argued that such a waiver is legal on the grounds that the existing CMS 1115 waiver authority extends to the drug rebate statute.

A related option would enable Medicaid to create a national coverage determination process, resembling Medicare's approach. State programs could refer products to a federal Medicaid coverage determination and could opt into its judgment (although this might require creating capacity in Medicaid to conduct such analyses). A narrower version of this approach would permit state Medicaid programs to adopt any national coverage determination issued by Medicare. The CMS might seek to do this using its existing authority under the Center for Medicare and Medicaid Innovation.

A key concern with such processes is to ensure that beneficiaries' interests are represented in coverage determinations because allowing for formulary exclusion may limit medication access for patients and undermine a key purpose of the accelerated approval program. However, just as other payers use the threat of exclusion to negotiate deeper discounts, state Medicaid programs may use the same strategy, meaning that access would not necessarily be limited. Other potential issues involve the administrative costs of establishing such a process and its potential breadth. For instance, although enabling state Medicaid programs to adopt Medicare's coverage determinations would be useful for a product like aducanumab, it would be less useful for products with high Medicaid market share but little Medicare exposure, such as eteplirsen or hydroxyprogesterone caproate.[6,22] Creating a Medicaid-specific coverage determination process at the federal level would permit state Medicaid programs to nominate for consideration products that are more important financially to the program.

Allowing state Medicaid programs to alter existing coverage requirements for accelerated approval products that have yet to show clinical benefits could be particularly effective in encouraging manufacturers to complete their confirmatory trials in a timely fashion. It could also enable Medicaid to act more quickly than the FDA if a drug were to fail its confirmatory trials because companies can often delay the FDA's withdrawal processes for years. One advantage of this proposal compared with others is that it is more feasibly implemented through administrative action without requiring statutory changes.

Medicaid Rebate Reform

MACPAC has proposed a second potential reform option to increase the mandatory minimum rebates owed to Medicaid for accelerated approval products. First, MACPAC proposed that accelerated approval drugs should be subject to an increased minimum rebate percentage on FDA approval. Once the FDA has granted the product a full approval after completion of confirmatory clinical trials, the minimum rebate percentage would then decrease to the otherwise standard level. Second, MACPAC proposed an increase in the inflationary rebate owed for accelerated approval drugs. This increase would go into effect only after a certain number of years if the manufacturer had not completed its confirmatory trials and obtained full approval from the FDA.[21] Depending on how high base rebates were increased, 1 study found that this proposal could save Medicaid $0.6 billion to $5.2 billion over 6 years, with additional savings of up to $0.9 billion from increased inflationary rebates.[23]

The MACPAC proposal would likely require legislation, and its effectiveness depends on the size of the increase in the rebates; however, this proposal is likely less administratively complex than other strategies because it builds on an existing rebate structure. The proposal targets products that have not yet converted to traditional approval and could encourage the timely completion of

confirmatory trials. This proposal seeks to lower Medicaid's costs for drugs without evidence of clinical benefits while also ensuring that patients in this critical safety net program will have access to potentially promising treatments.

Value-Based Pricing

A third reform option would set reimbursement rates for accelerated approval drugs based on cost-effectiveness and comparative-effectiveness analyses. This approach would examine the existing clinical evidence supporting a particular product to ascertain a reimbursement rate at which the drug represents a fair value for the health care system. This approach includes comparing the clinical evidence for a novel drug with evidence that supports existing drugs for the same condition to assess whether the novel drug is likely to be superior, which would justify a higher price. These approaches are used by many other countries to ascertain appropriate pricing for new drugs,[24] and they permit payers to balance the prices that are paid while clinical evidence develops.

Using this approach, Medicaid programs would be authorized to establish reimbursement offers after considering the clinical benefits of accelerated approval products at the time of approval. This proposal has been advanced by the Medicare Payment Advisory Commission,[25] but it could also be applied to Medicaid. Additional challenges would be present in the Medicaid context: it is not clear that each state's Medicaid program has or should develop the internal capacity to perform this type of analysis. The CMS may wish to perform this analysis at the federal level, permitting states to opt in as they choose.

A value-based pricing proposal could address several criticisms of the accelerated approval program. Like other proposals, it could encourage manufacturers to complete confirmatory trials more quickly to gather evidence necessary to establish higher reimbursement rates. Such a proposal should also enable Medicaid to critically examine those products whose confirmatory trials are based on surrogate end points. Manufacturers of those products need to show clinical benefits to command higher prices. The CMS might seek to implement this strategy using its existing Center for Medicare and Medicaid Innovation authority, although statutory change could be more effective in providing the agency with funding and expertise to grow the program over time.

Consolidated Purchasing or Carve Outs

A fourth potential reform option would take inspiration from existing proposals to create a federal insurance program for select products, especially cell and gene therapies for rare diseases.[26] Given their high per-patient prices, having even a small number of patients who need such products can create financial uncertainty for state Medicaid budgets. The goal would be to shift the financing of these medications to the federal government by increasing the federal share of Medicaid spending to 100% either for all accelerated approval products or rare disease products alone. Under some of these proposals, access could be managed through a rare disease fund for all patients regardless of payer type.

The key benefit of this proposal would be to provide access to accelerated approval drugs for patients while insulating states from the uncertainty and cost of reimbursement. Therefore, the proposal primarily shifts costs and does not inherently respond to criticisms of the program, but it could serve as a platform to do so. For instance, the federal government might demand value-based pricing from manufacturers as a condition of reimbursement under the program, or it could demand greater pricing concessions if purchasing is centralized rather than fragmented across states and payers. However, legislation would likely be required to create such a program.

Discussion

These 4 reform proposals share several opportunities as well as challenges. Each option has the ability to respond to many of the core criticisms of the accelerated approval program, although value-based pricing is likely the strongest proposal because of its responsiveness to the quality of the

confirmatory trials involved. One potential operational challenge of all the proposals is the difficulty of reforming reimbursement for products approved for multiple indications (some indications with accelerated approval and others with traditional approval). The state-based administration of Medicaid may make it challenging to implement reforms that centralize authority with CMS, such as those with a national coverage determination context. The political resistance to and practical difficulties of capacity building, particularly around value-based pricing, may serve as additional barriers to change. But given the burdens that states face at present—burdens that may grow if the FDA's operations of the program are not subject to reform—identifying proposals, such as those described herein, is important to ongoing reform efforts.

Conclusions

In addition to ongoing proposed reforms to the FDA's operation of the accelerated approval pathway, policy makers may wish to consider options for reforming payer reimbursement for these products. The types of proposals that we have described could provide a range of options for policy makers to evaluate trade-offs of access and pricing associated with the accelerated approval program.

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