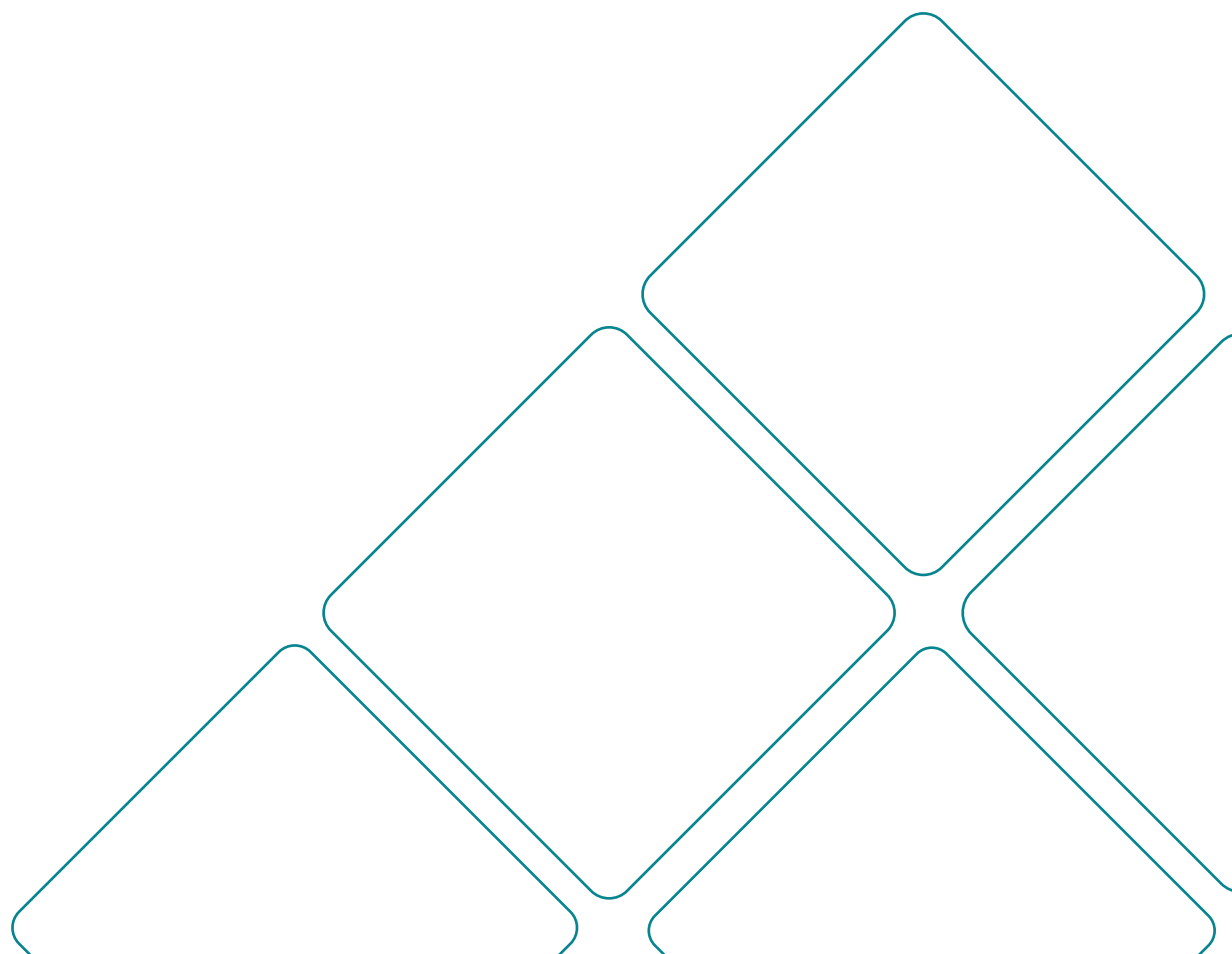


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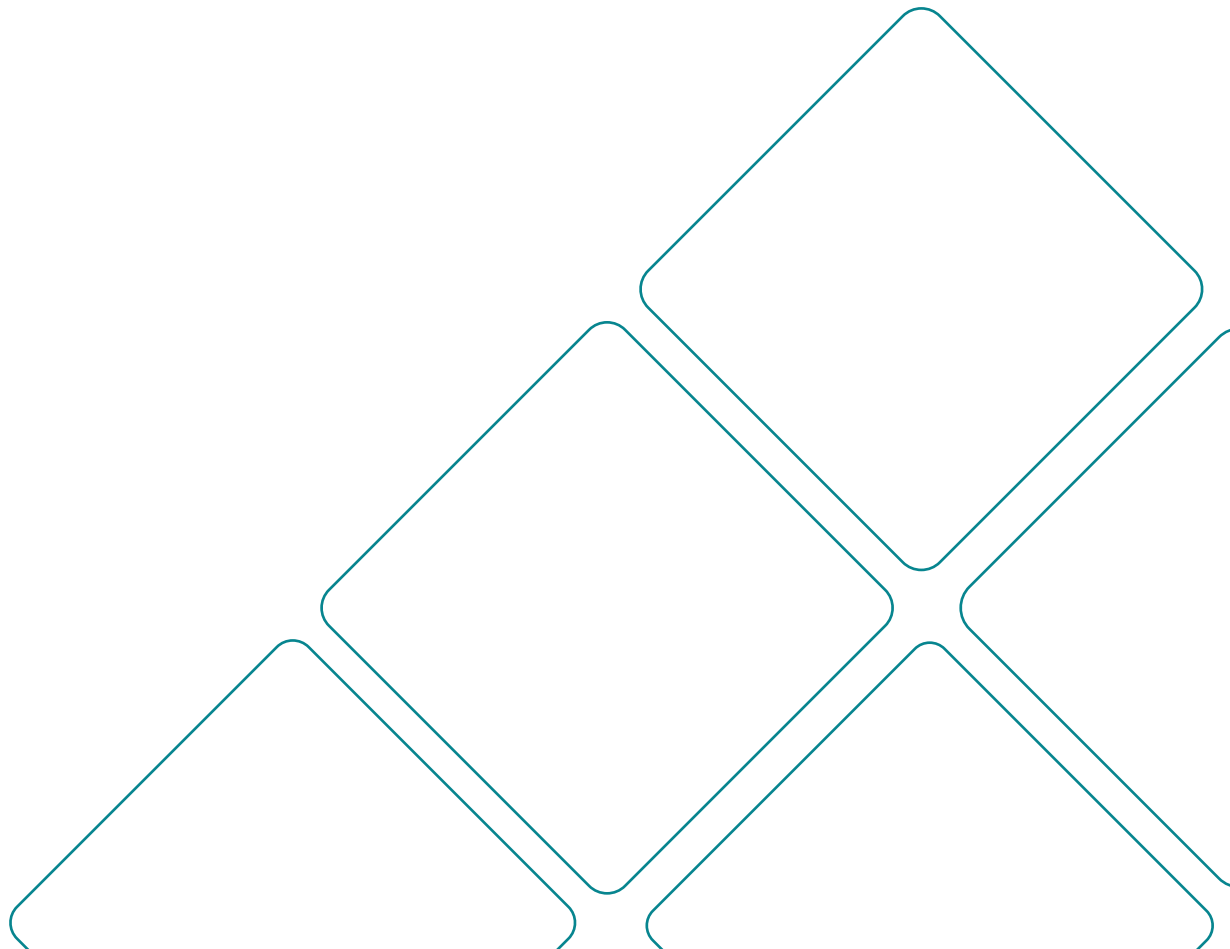
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Prescription Drug Pricing: A Health Affairs Collection
Alan Weil, Editor-In-Chief

The People-to-People Health Foundation, Inc. (Project HOPE), Millwood, Virginia
Health Affairs Editorial Offices: Bethesda, Maryland
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Published by Project HOPE
7500 Old Georgetown Road, Suite 600
Bethesda, Maryland 20814-6133
Tel: 301-656-7401
Fax: 301-654-2845
www.healthaffairs.org

Cover and layout design by Julia Vivalo, Health Affairs.

Printed and bound in the United States of America.

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EXPEDITED APPROVAL PATHWAYS

For drugs of particular clinical importance, the Food and Drug Administration offers several expedited development and approval pathways.

The use of expedited drug development and approval pathways, such as Accelerated Approval and Breakthrough Therapy Designation, raises important issues related to pricing policy. For example, the foreshortened development and approval process translates into potentially significant economic advantages to drug developers; these, in turn, could support arguments that the resulting prices should be lower. Conversely, the pathways are intended to support rapid development of drugs that offer significant advantages over available therapies for serious medical conditions—circumstances that would suggest that the resulting therapies may deliver high value that justifies high prices.

Background

The Federal Food, Drug, and Cosmetic Act requires new drugs to show “substantial evidence” of efficacy before approval by the Food and Drug Administration (FDA). Historically, the FDA has interpreted that standard to encourage at least two rigorous clinical trials (preferably randomized, double-blind, placebo-controlled studies) that independently show a statistically and clinically meaningful benefit.

Even as that historical standard developed, the FDA has always made exceptions in cases of serious, unmet need. In the 1980s the AIDS epidemic heightened the need for a formal process to expedite drug approval in the face of poorly treated, life-threatening diseases. To that end, the FDA and Congress created several pathways including Accelerated Approval and Breakthrough Therapy Designation, intended to help shorten the drug development and approval timeline and make new therapies available more rapidly. Such pathways can provide significant economic benefits to drug developers by reducing the cost of premarket studies and allowing earlier market entry. Compared to the traditional model, the pathways also involve different types and levels of clinical evidence of efficacy, thereby increasing uncertainty about claimed benefits and safety of the therapies.

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Accelerated Approval: Brief History

Accelerated Approval (AA) was created by FDA regulation in 1992, in response to the emergence of the AIDS epidemic. It was codified by the FDA Safety and

Innovation Act (FDASIA) in 2012. Using AA, the FDA may grant approval for a new drug that offers a significant benefit compared to available therapies for serious medical conditions where there is unmet medical need, based on preliminary evidence of efficacy. The sponsor must then conduct definitive efficacy trials (called “confirmatory studies”) after approval.

“Should shorter development time mean lower prices?”

That model worked well for antiretroviral medicine, allowing approval of therapies based on short-term studies using easy-to-measure “surrogate markers” of efficacy, such as lowered CD4 blood cell counts. Recently, AA has been applied most commonly in oncology, with drugs approved based on short-term studies measuring early indicators of efficacy, such as tumor shrinkage, with later confirmatory studies showing improved survival or durable stabilization in disease.

According to the FDA, from 2012 to 2016 [twenty-six new molecular entities](#) were initially approved using the AA pathway—about 13 percent of total FDA drug approvals during that period.

■ The Accelerated Approval Process

There are several important elements in the AA process.

USE OF SURROGATE ENDPOINTS

Accelerated Approval is often equated with approval based on surrogate markers. However, the two are not the same. Outside of the AA process, the FDA routinely grants approval of drugs based on surrogate endpoints, when the agency believes that the connection between the surrogate endpoint and the desired clinical outcome is well established. For example, the FDA approves hypertension therapies that lower blood pressure (the surrogate endpoint) without requiring evidence that the therapies reduce cardiovascular disease (the desired clinical outcome).

Under the AA pathway, the FDA can base approval

on a surrogate marker when the agency does not consider the connection to clinical benefit to be as fully established as it is in the hypertension example. Instead, according to FDA guidance for the industry, the marker must be “reasonably likely” to predict improved clinical outcomes. That standard has never been formally defined. Thus, there is considerable variation and discretion on when a given biomarker “counts” as an acceptable surrogate for AA.

The AA process also allows the FDA to base approval on an “intermediate clinical endpoint,” envisioned as a short-term treatment effect on a clinical outcome that is then confirmed in longer-term studies after approval. The decision about whether a given effect qualifies as an “intermediate” clinical benefit is made largely case by case.

GRANTING OF FULL APPROVAL

In crafting the regulations, the FDA specifically avoided defining AA as “conditional approval” or otherwise suggesting that the drug is not fully approved. The semantics are important, both for the FDA’s ability to enforce post-approval study requirements and for securing insurance coverage, since many health plans only cover drugs for FDA-approved uses.

“STREAMLINED” WITHDRAWAL

The AA pathway includes a process for “streamlined” withdrawal of a drug’s approval in the event that subsequent trials fail to confirm clinical benefit. In practice, however, the streamlined withdrawal process has not worked much differently than the process the FDA follows in any other case where it concludes that a product should be withdrawn from the market for safety or efficacy reasons. To date, there has only been one example of the FDA’s formally invoking the AA withdrawal process, leading to the removal of the indication for use of Roche/Genentech’s Avastin (bevacizumab) for metastatic breast cancer in 2011.

■ Breakthrough Therapy: Brief History

The Breakthrough Therapy pathway is a newer regulatory invention than the Accelerated Approval pathway, having been enacted in FDASIA in 2012. The idea was developed via several interdisciplinary

workshops hosted by the patient advocacy organization [Friends of Cancer Research](#) and the Brookings Institution.

The goal was to identify therapies offering significant advances in difficult-to-treat cancers early in development, thereby shortening the clinical trial stage. Patient advocates argued that when new, targeted therapies appear to offer unprecedented efficacy, traditional clinical development programs might needlessly expose clinical trial subjects to ineffective or outdated therapies. FDASIA explicitly directed the FDA to consider this potential impact on clinical trial participants when granting Breakthrough status.

■ The Breakthrough Therapy Process

There are a number of important elements in the Breakthrough Therapy Designation process.

PRELIMINARY CLINICAL EVIDENCE

The Breakthrough pathway involves a formal request by a sponsor for designation, which can be submitted any time during clinical development, up to the time of the filing of the marketing application. To grant Breakthrough status, FDA guidance explains, the agency must find that there is “[preliminary evidence that the drug offers a “substantial improvement”](#)” on at least one clinically significant endpoint over existing therapy. That standard is necessarily subjective and is the main reason that, according to the FDA, most Breakthrough Therapy Designation requests are [rejected or withdrawn](#).

UNCLEAR IMPACT ON REGULATORY PROCESS

FDASIA lists steps that the FDA “may” take in reviewing Breakthrough applications, including meetings with sponsors and “timely advice” to ensure an efficient development process. Those obligations are not unique to drugs granted Breakthrough status, however. In addition, unlike many other FDA activities, there are no defined metrics for the FDA to meet for Breakthrough products, such as timelines for scheduling meetings and providing written advice. Thus far, however, the FDA has embraced the spirit of the legislation, with [sponsors reporting](#) enhanced interactions with the agency for products gaining Breakthrough Therapy Designation.

INCREASING USE OF THE PATHWAY

Breakthrough status is far more common than anticipated. The FDA has received over 100 designation requests per year. There are more than 175 drugs and biologics with Breakthrough Therapy Designation, including new indications for already-approved products. While the largest proportion is in oncology, there are designated Breakthrough therapies in all FDA review divisions.

Since 2012 [twenty-nine new molecular entities](#), or about 13 percent of all FDA drug approvals, have received Breakthrough Therapy Designation. However, most of those approvals were for applications that were in advanced development before the pathway was created; those products may have benefited from Breakthrough-style engagement by FDA, but not literally from Breakthrough status itself.

■ Key Questions For Drug Pricing And Coverage Policy

There are several outstanding questions about how or whether expedited approval pathways should affect drug prices and coverage policy.

SHORTER DEVELOPMENT TIME

Should shorter development time mean lower prices? Drug developers have historically cited the high cost of research and development and the long lead time to bring a product to market as factors justifying the price of innovative therapies. Thus, the use of expedited pathways could support an argument that the resulting therapies should be priced lower than they otherwise would have been if they did not benefit from these pathways. A related argument is that the FDA’s efforts to expedite development and approval impose a reciprocal obligation on the new drug sponsor to price affordably—[analogous to the claim that products of taxpayer-funded research should be subject to increased pricing oversight](#).

The counterargument is that the Accelerated Approval and Breakthrough pathways are reserved for therapies that offer significant potential benefits for unmet medical needs—and are therefore at the high end of the value spectrum for new therapies. That

might argue that payers should accept higher prices for expedited therapies.

IMPACT OF UNCERTAINTY

Should pricing and coverage policy reflect the uncertainty of pending confirmatory trials? Expedited pathways involve different types and levels of premarket evidence at the time of approval than do standard pathways. As a result, there may be less safety information than is the case for most newly approved therapies, which increases the risk of unexpected findings after approval. Those concerns were highlighted in a [2015 Government Accountability Office \(GAO\) report](#).

For Accelerated Approval therapies in particular, there may also be considerable uncertainty in the efficacy data at the time of approval. While the FDA has always carefully defined those drugs as fully approved, some payers may take a different approach in their coverage policies. In a rare example of this dynamic, some insurers recently took the position that Sarepta's Exondys 51 (eteplirsen), granted Accelerated Approval to treat Duchenne muscular dystrophy, should still be considered "experimental" for coverage purposes.

ENFORCEMENT OF CONFIRMATORY STUDIES

Can the FDA enforce confirmatory studies? The agency has been challenged to ensure that "mandatory" postmarket confirmatory studies are completed in a timely fashion. The gaps in that process were highlighted in a [2009 GAO report](#). One option is to give the FDA enforcement tools (such as civil monetary penalties) that are less blunt than the withdrawal of approval of the underlying application. The FDA already has the authority to fine manufacturers for failure to meet timelines for mandatory safety

studies. Another option would be to create a formal "conditional" approval process, whereby the underlying license to market the new drug will expire unless confirmatory studies are submitted on time.

Key Terms

- **Substantial evidence of efficacy:** "Evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof." (*FDA Guidance for Industry: Expedited Programs for Serious Conditions—Drugs and Biologics, May 2014*)
- **Surrogate endpoint:** "For purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure, that is thought to predict clinical benefit, but is not itself a measure of clinical benefit." (*New Drugs, 21 U.S. Code Sec. 355, 2010*)
- **Confirmatory studies:** Sponsors of drugs granted Accelerated Approval are required to conduct post-approval studies "to verify and describe [a drug's] clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome." (*Applications for FDA Approval to Market a New Drug, 21 CFR 314, 2016*).

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Cite as: "Health Policy Brief: Expedited Approval Pathways," *Health Affairs*, July 21, 2017. DOI: 10.1377/hpb2017.2

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PRICING ORPHAN DRUGS

A 1983 law created incentives to develop drugs to treat rare diseases that might otherwise not justify commercial investment.

Many of the drugs developed by companies relying on incentives created by the Orphan Drug Act have high prices. This has made the law controversial, though the relationship between those high prices and the incentives in the law is not always clear. One prominent incentive in the Act is a special period of market exclusivity that prohibits the Food and Drug Administration (FDA) from approving a competing version of the drug for seven years—in essence, a statutory protection that increases pricing power for a drug marketer. In some prominent cases, however, the orphan drug exclusivity has been used to provide protection for drugs that have been available in unapproved forms for many years. The resulting increase in the price of those products has garnered significant attention from policy makers and the public.

Background

The [Orphan Drug Act of 1983](#) created a class of therapies defined not by biology or medical specialty, but by the prevalence of the treated condition in the population. The act was driven by concern that pharmaceutical companies would not develop drugs to treat diseases with a small number of patients and therefore a limited commercial market. Examples of diseases to which the Orphan Drug Act applies include cystic fibrosis and muscular dystrophy.

The law established economic incentives—including tax credits, research grants, and special market exclusivity protections—to encourage drug developers to invest in drugs for rare diseases. Market exclusivity was believed to be particularly important for orphan drugs at the time of the law's passage. Then as now, most new pharmaceuticals have patent protection at the time of approval, which blocks competition broadly. The exclusivity provision in the Orphan Drug Act was intended to offer nonpatent (statutory) protection against competition to encourage companies to invest in products that do not have patents or where there might be questions about the ability to enforce a patent.

Since 1983 the FDA has granted more than 3,500 orphan “designations” (see below) and approved more than 500 orphan drugs. Recently, as the biopharma business model has evolved and the science of targeted therapies has advanced, orphan drug designations have increased dramatically. The FDA [received](#) a record 440 requests for such designation in FY 2015, more than double the

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number five years ago. This has occurred even though the threshold for orphan status is fixed at 200,000 patients, and is therefore an ever smaller percentage of the growing US population.

The Orphan Drug Act was supported by the [National Organization for Rare Disorders](#), a coalition built on the premise that because there are so many different

the idea of a sponsor that actually intends to market a drug for a large patient population—for example, people with lung cancer—but seeks orphan designations first for one slice of the market (stage 4 lung cancer), then for another (stage 3).

As understanding of genomic markers of disease has advanced, there have been new questions about when a specific subset of a common disorder should qualify for orphan status. The FDA [updated](#) its orphan drug regulations in 2013, defining a new concept for designation requests, known as an “orphan subset,” for determining when a specific use is or is not an appropriate orphan indication.

A single product can have multiple orphan designations for different rare diseases and can also be approved for use in non-orphan diseases. Sponsors with an orphan drug designation receive tax credits to support clinical development and are eligible for grants administered by the FDA. Upon approval, an orphan drug is awarded seven years of “market exclusivity,” meaning that no other sponsor can market the same drug for the same orphan-designated use. (The same drug can be marketed by a different sponsor for *other* uses, and *different* drugs can be marketed for the same orphan use.)

Another provision allows the FDA to approve the same drug for the same orphan-designated use if a sponsor demonstrates that its product conveys a clinically meaningful benefit, compared to the already marketed version. Those exceptions (known as “breaking” the orphan exclusivity of the first product) are rare and generally relate to differences in the formulation that may affect safety, efficacy, or convenience.

“A single product can have multiple orphan designations for different rare diseases.”

rare diseases, collectively they have a broad societal impact. Those advocates view the law as a success—one reason the market exclusivity approach has been imitated in other incentive programs enacted over the past three decades (Exhibit 1).

However, the Orphan Drug Act has also generated debate, often tied to the very high prices of many drugs for rare diseases. In some cases, the price of an orphan drug may limit access for the patients the law is intended to serve. Even when the direct cost to patients is low (because of insurance, patient assistance programs, or both), the commercial success of some orphan drugs calls into question the need to incentivize their development in the first place.

■ The Orphan Drug Act: What You Need To Know

Sponsors may request, and the FDA generally grants, an orphan drug designation for any product intended to treat a disease that affects fewer than 200,000 patients in the US. (The law also allows a designation for a disease that affects more than that number if a sponsor can demonstrate that a potential treatment would not make a profit. The latter approach has been used only a handful of times.) In some instances, there have been disagreements about whether a proposed patient population has been defined arbitrarily to create an orphan indication—a practice referred to as “salami slicing.” The metaphor is intended to convey

■ Important Concepts For Pricing And Coverage Policy

Several important concepts relate to how (or whether) orphan drug status affects prices and coverage policy.

VARIED UNDERLYING PRICING DYNAMICS

Orphan drug status applies to diverse products with different pricing dynamics, complicating efforts to craft policies to address costs. In contrast to

expedited pathways such as [Accelerated Approval](#) or [Breakthrough Therapy Designation](#), orphan drug status is not tied to the severity of the disease or the perceived effects of the therapy; instead, it is simply a matter of counting potential patients. A drug to treat a mild condition can qualify, as can a drug that offers only mild symptomatic benefits for a serious disease.

Further complicating pricing, many orphan approvals are new indications for drugs with broader approved uses; for example, the top-selling drug in the world, AbbVie's Humira (adalimumab), has several orphan drug indications but is also approved for arthritis and related rheumatology uses. In those cases, pricing reflects the dynamics of the broader market, not the rare disease use.

Drugs approved exclusively for rare diseases often have extremely high prices (hundreds of thousands of dollars per patient per year). Sponsors may explain

those prices by citing the need to generate an appropriate return on investment based on the costs of development. However, there are a number of examples of drugs approved solely for orphan indications that generate sales in excess of \$1 billion annually—a common standard for commercial success for products intended for common diseases. While those are a relatively small number of the 500 orphan drug approvals, they call into question the underlying premises of the incentives: that there is no viable commercial market to treat rare diseases.

VALUE OF MARKET EXCLUSIVITY

Despite the long-standing view of the value of market exclusivity, the seven-year protection has become less important over time, resulting from subsequent changes in market protections for all new therapies. In fact, most successful orphan drugs do not rely on these protections. The 1984 Hatch-Waxman Act gives *any* never-before-approved drug a minimum

EXHIBIT 1

Exclusivity Incentives For Drug Developers

Type/Legislation	What Products Qualify?	Scope Of Exclusivity	Duration
Orphan drug Orphan Drug Act, 1983	Drugs to treat diseases affecting fewer than 200,000 patients in the US, or for which there is "no reasonable expectation that the cost of developing and making available" the therapy will be recovered.	The FDA cannot approve the same drug for the same use until exclusivity expires, unless the second applicant can show clinical superiority to the first.	7 years
New molecular entity Hatch-Waxman Act, 1984	Drugs with "an active ingredient that has never before been marketed in the U.S. in any form."	The FDA cannot receive an Abbreviated New Drug (generic) Application (ANDA) until exclusivity expires.	5 years <i>(4 years if the ANDA is challenging a patent)</i>
New formulation Hatch-Waxman Act, 1984	New formulations of previously approved drugs that require clinical data to support approval.	The FDA cannot approve a generic application until the exclusivity expires.	3 years
Innovator biologic Affordable Care Act, 2010	Novel biologic therapies, upon FDA approval.	No biosimilar application may be approved until exclusivity expires.	12 years
Pediatric exclusivity FDA Modernization Act, 1997	Any new drug for which a sponsor completes a pediatric study subject to an FDA written request.	Added to all patent and exclusivity protections. Each new drug is eligible for only one extension.	6 months
Qualified infectious disease product FDA Safety and Innovation Act, 2012	New antibacterial or antifungal drugs intended to treat serious or life-threatening infections.	Added to all other exclusivities.	5 years
Single-enantiomer products FDA Amendments Act, 2007	Single-isomer formulations of drugs previously available solely as racemic mixtures.	The same protection as the new molecular entity exclusivity.	5 years

SOURCE Prevision Policy LLC.

five-year exclusivity period for all uses—which in practice typically means at least a seven-year period before generic competition can begin.

The law also provides for restoration of patent life to make up for time in development and under FDA review, so a product with any remaining patent life at the time of FDA approval is almost certain to have a patent term longer than the seven-year orphan protection. In addition, the biosimilar provisions in the Affordable Care Act (ACA) give new biologic medicines a minimum twelve-year exclusivity period. As a result, most drug developers—whether granted orphan status or not—can be assured of at least seven years of exclusivity for any novel molecule or biologic.

CONTROVERSY AROUND MARKET EXCLUSIVITY

Drugs that *do* depend on market exclusivity have been controversial. KV Pharma's preterm labor drug Makena (4-aminopyridine, or 4-AP) and Marathon's steroid approved for Duchenne muscular dystrophy, Emflaza (deflazacort), are recent examples in which sponsors sought orphan status and subsequent FDA approval for therapies that many patients were accessing previously in unapproved forms (pharmacy compounding for 4-AP and importation from Europe for deflazacort).

The seven-year market protection was a key factor in the decision to seek FDA approval with orphan status, since neither product had patent protection that would otherwise allow a premium price. Both

sponsors faced significant resistance from patients and payers based on the much higher price point compared to the older source of supply. That has led to the unusual dynamic of patient and consumer advocates urging the FDA to allow continued access to an "unapproved" product instead of using its enforcement powers to cut off the alternative supply once an approved version is available.

ADDITIONAL BENEFITS OF ORPHAN STATUS

Orphan drug status conveys other benefits not originally included in the law. Sponsors of applications for orphan drugs are exempt from user fees to support that review. Although user fees did not exist at the time of the 1983 Orphan Drug Act, non-orphan sponsors now pay a fee of more than \$2 million for review of a new drug application. The ACA also exempted products with an orphan drug designation from otherwise mandatory discounted pricing for certain payers under the federal [340B drug pricing program](#).

In addition, the ACA exempted drugs that are approved solely for orphan indications from their portion of the [annual market-share fee](#) paid by pharmaceutical companies. (The annual fee, negotiated by the pharmaceutical industry as part of the ACA debate, amounted to a total of \$4 billion in 2017.) Finally, developers of drugs to treat rare diseases receive enhanced attention within the FDA from a dedicated office for orphan products and a rare disease specialist.

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Cite as: "Health Policy Brief: Pricing Orphan Drugs," *Health Affairs*, July 21, 2017. DOI: 10.1377/hpb20173

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BIOSIMILARS

Follow-on products to innovative brand-name biologic medicines may lower overall drug spending by creating price competition.

The recent rise of biologic medicines has produced a wave of new therapies. **Biologics** include a range of products, including vaccines, recombinant therapeutic proteins, blood and blood components, gene therapies, and others. These new medicines—most of which are complex molecules more difficult to produce than traditional, small-molecule drugs—are important medical advances, but they have driven prescription drug spending higher overall. The hope is that biosimilars—follow-on products to innovative branded biologics—will lower overall drug spending by creating price competition for those biologics in the same way generic drugs compete with traditional branded medicines. However, unlike generic drugs, where substitution of the generic for the brand name is embedded in practice through state laws and health plan policies, the launch of a biosimilar does not trigger pharmacist substitution of the biosimilar for the original biologic—the primary mechanism that creates price competition for small-molecule drugs. The impact of biosimilar development on pricing may therefore be much less substantial than the impact of generic drugs—at least for the foreseeable future.

Background

The 1984 generic drug law, known as the **Hatch-Waxman Act**, plays an important role in promoting price competition once brand-name drugs lose patent protection. The law, however, does not apply to biologic medicines, which account for a growing proportion of the top-selling prescription drugs in the US. In 1984 the biotechnology sector was in its infancy, and the primary medicines regulated as biologics were vaccines or drugs derived from human blood (such as hemophilia clotting factors). By the 2000s, however, biologic medicines were increasingly common as therapeutics. Congress recognized that a process to copy those therapies would be more complicated than the process for small-molecule drugs, which are structurally simpler.

Under the Biologics Price Competition and Innovation Act (BPCIA) of 2010 (part of the Affordable Care Act), Congress created an abbreviated Food and Drug Administration (FDA) approval pathway for “biosimilar drugs”—versions of biologics made by manufacturers other than the original innovator. The goal was to open up price competition for biologic therapies after their patents expired. While the approach is patterned on the generic drug process, the new pathway reflects the greater complexity of the underlying products and the associated

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challenge of ensuring that the safety and efficacy of “copies” match that of the innovator drug.

The chemical and molecular makeup of biologics is critical to understanding the differences between the generic and biosimilar regulatory models. Generics are chemically equivalent and bioequivalent—that is, the drugs have the same active ingredient and are absorbed in the patient’s bloodstream at the same rate as the branded small-molecule drugs they copy. Biologics are significantly larger, more complex molecules, which makes them scientifically difficult to fully replicate. As a result, the biosimilar pathway requires functional or clinical equivalence, rather than chemical equivalence.

The impact of the Hatch-Waxman Act underscores the potential, future impact of the biosimilar drug pathway. According to a Congressional Budget Office study, **generics made up about 20 percent** of the US prescription drug market at the time of the act’s passage but now represent almost 90 percent of that market. According to the FDA, consumers pay roughly **80–85 percent less** for a generic compared to the brand. No one expected the biosimilar pathway to have that level of impact right away. The FDA, in particular, has moved cautiously in the use of the pathway, with an emphasis on safety. In addition, ongoing litigation has delayed or blocked market entry for the first wave of products born out of the BPCIA.

There have been five biosimilars approved (with two launched commercially) since the BPCIA was enacted (Exhibit 1). These products will likely offer competition more akin to “me too” brands (chemically similar, but not identical, drugs that treat the same disease with no demonstrably different properties) than to generics.

The Biosimilar Approval Process

There are several important elements in the biosimilar approval process.

DIFFERENT STANDARDS OF APPROVAL

The biosimilar pathway requires the FDA to approve therapies based on a different standard than it uses for new drugs (including biologics), which generally requires human trials to prove safety and efficacy. The standard is also different from the one used by the FDA for approval of generics, which usually requires a small human study measuring blood levels of the active ingredient compared to the brand, to prove “bioequivalence.” Short comparative studies of the generic drug’s activity in healthy volunteers typically suffice for FDA approval.

Unlike generic drugs, biosimilars do not have to meet a standard of bioequivalence to the reference product. Instead, the legal standard laid out in FDA guidance is that biosimilars must be “**highly similar**” to the reference product, notwithstanding minor differences in clinically inactive components. Furthermore, there may be no clinically meaningful differences between the biosimilar and reference products in terms of safety, purity, and potency. The FDA applies a “step-wise approach” to reaching that standard, with early characterization of the biosimilar through analytical and animal studies and (usually) at least one clinical study. At every step, the biosimilar sponsor must analyze the extent of any residual uncertainty about the biosimilarity of the product to the reference product and determine steps to resolve it.

EXHIBIT 1

FDA-Approved Biosimilars

Biosimilar	Reference Innovator	Approved	Launched
Sandoz’s Zarxio (filgrastim-sndz)	Amgen’s Neupogen	2015	Yes
Celltrion’s Inflectra (infliximab-dyyb)	Johnson & Johnson’s Remicade	2016	Yes
Sandoz’s Erelzi (etanercept-szsz)	Amgen’s Enbrel	2016	No
Amgen’s Amjevita (adalimumab-atto)	AbbVie’s Humira	2016	No
Samsun Bioepis’s Renflexis (infliximab-abda)	Johnson & Johnson’s Remicade	2017	No

SOURCE Prevision Policy LLC; FDA and company press releases.

“INTERCHANGEABILITY” AND SUBSTITUTION

When bioequivalent generic drugs are approved by the FDA, state laws permit (and usually encourage) pharmacists to substitute generic for brand-name products without contacting the physician. This is a critical reason that prices for pharmaceuticals drop rapidly after generic entry.

An FDA-approved biosimilar, however, is not automatically deemed interchangeable with the brand-name biologic and cannot be substituted without physician approval. Interchangeability requires a second determination above the finding that it is “highly similar” to the reference product. FDA’s [draft standard for interchangeability](#) indicates that the risk of “switching between use of the [biosimilar] product and its

“Many states have passed laws carving out biosimilars from drug substitution laws.”

reference product is not greater than the risk of using the reference product without such alternation or switch.” There have been, to date, no biosimilars deemed interchangeable with innovator biologics. In addition, many states have passed laws carving out biosimilars from drug substitution laws, essentially blocking pharmacist substitution even if the FDA deems a biosimilar interchangeable.

Another challenge for substitutability is the FDA’s [policy](#) that biosimilars carry a unique nonproprietary name compared to the branded product, so regulators, physicians, pharmacists, and consumers can distinguish between the two. Specifically, manufacturers must apply a four-letter “nonsense” suffix to the nonproprietary name of biologics. For example, for the biologic adalimumab (sold as brand-name Humira), the biosimilar will be called “adalimumab-atto.” According to the FDA, “Distinguishing suffixes should help minimize inadvertent substitution of any such products that have not been determined to be interchangeable.”

TWELVE-YEAR MARKET EXCLUSIVITY

Protecting incentives for development of new biologics was a high priority for legislators—and a subject of considerable debate—when Congress designed the biosimilar pathway. The new law precludes approval of a biosimilar application until twelve years after the date on which the reference product was first licensed. That is substantially longer than the five-year protection (four years if a patent is challenged) for brand-name pharmaceuticals under the Hatch-Waxman Act.

THE “PATENT DANCE” CAN CAUSE DELAYS

The biosimilar pathway includes a unique process for resolving patent disputes prior to the potential approval of a biosimilar application. In what is referred to as the “patent dance,” biosimilar and reference-product sponsors must exchange intellectual property information and work through patent disputes according to a schedule. In theory, the process assures smoother, more predictable entry for biosimilar products than has been the case with the Hatch-Waxman generic drug patent challenge system. However, the ground rules for the patent dance have already generated litigation that has been brought to the [Supreme Court](#), which [ruled in June 2017](#), in *Sandoz Inc. v. Amgen Inc.*, that the patent dance is optional under federal law.

■ Key Questions For Drug Pricing And Coverage Policy

There are several outstanding questions about how or whether the biosimilar pathway should affect drug prices and coverage policy.

UNCERTAIN COMPETITIVE IMPACTS

It is unclear whether more biosimilars will lead to lower prices. Prior experience with generic drugs suggests that prices come down to about half the original price when there are at least two competitors, and to as low as one-third when there are a half-dozen fully interchangeable, competing products. It remains an open question whether a similar level of price competition will emerge for biologics. Biosimilar developers argue that without interchangeability, there will likely never be such price reductions for biologics. The first

biosimilars (Exhibit 1) were launched commercially in the US at modest discounts (in the range of 15–20 percent) from the reference product. For the foreseeable future, given the small number of biosimilars approved, the competitive landscape for biologics won't likely differ from that of a brand-versus-brand market.

THE ROLE OF MEDICARE PART B

Some stakeholders believe that Medicare payment policy should address the cost of biologics more directly. The biosimilar law includes provisions related to Medicare Part B, which covers physician-administered drugs and is an important market for many biologics used for cancer and rheumatology. Medicare is prohibited from applying the same payment to a biosimilar and an innovator drug. Instead, the program must have separate payment codes for the biosimilar and the innovator, albeit with a formula intended to minimize incentives for physicians to choose the brand over the biosimilar (physicians are paid a percentage of the brand price, not the biosimilar price, if the biosimilar is prescribed). In theory, combining the brand and biosimilar products under a single payment code would do more to encourage price competition.

The provider would receive the same reimbursement no matter which therapy is used and thus would have an incentive to choose the lowest-cost agent.

SUBSTITUTION WITHOUT INTERCHANGEABILITY?

The initial FDA approvals have been for noninterchangeable biosimilars, which typically means that the prescriber will have to select the biosimilar for it to be dispensed. There have been some efforts to revise state pharmacy laws to treat biosimilars as interchangeable for substitution purposes, but those have been largely unsuccessful and are opposed by the FDA. However, physicians are now increasingly accountable for drug costs under capitated or bundled payment arrangements, particularly for conditions (such as cancer) in which biologics are used. Payers may therefore be able to encourage providers' adoption of biosimilars, even without interchangeability.

The Centers for Medicare and Medicaid Services has also supported policies to promote biosimilar adoption by Medicaid and Medicare Part D, including a policy allowing Part D plans to limit formularies to include only the biosimilar when one is available.

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Cite as: "Health Policy Brief: Biosimilars," *Health Affairs*, July 21, 2017. DOI: 10.1377/hpb20174

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PATENT SETTLEMENTS

The timing of a generic drug's market entry may be determined by "pay for delay" patent settlements between drug companies.

The generic drug sector in the US helps hold down pharmaceutical costs, with prices of widely used drugs typically dropping to commodity levels once multiple-generic competition begins. In some cases, the innovator (brand-name) company can settle patent litigation with a single generic drug firm by negotiating a payment to the challenger in exchange for agreement on a set, future date for generic entry—and, in the process, blocking all other generic launches of the same drug. That, in turn, delays the start of the erosion in the brand-name price—even in cases where the underlying patents are eventually deemed invalid. These so-called pay-for-delay agreements have been challenged by antitrust regulators with some success. However, federal courts have not agreed with antitrust authorities that there should be a bright-line rule defining those agreements as anticompetitive, prompting proposals for legislation to address the issue directly.

Background

The 1984 Drug Price Competition and Patent Term Restoration Act (known as the [Hatch-Waxman Act](#)) instituted a process for identifying and litigating innovator companies' patent claims to determine when a generic firm can launch a competitor.

One byproduct of the Hatch-Waxman Act is the emergence of settlements to resolve patent lawsuits whereby a brand company and a single generic firm agree on a generic launch date months or years in the future and, in the process, block any other generics from coming to market. The settlements often involve a payment from the innovator company to the generic firm, called a "reverse payment." These settlements are referred to as pay-for-delay agreements because they postpone the start of generic competition later than the date the generic company asserted in litigation that it should be able to launch if the patents in question are overturned.

Settling companies argue that the agreements are appropriate and pro-consumer: Typically, the generic can come to market before the expiration date of at least one patent at issue, and the certainty of the timing benefits purchasers. Litigation settlements, by their nature, involve compromise, and settling companies reject the description that the agreement is pay-for-delay. Consumer

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advocates, however, argue that the settlements are anticompetitive and keep drug prices higher than they would otherwise be. The Federal Trade Commission (FTC) [agrees](#), having brought multiple cases challenging the settlements over the past two decades.

However, the FTC has not persuaded federal courts to draw a bright line defining agreements involving reverse payments as presumptively anticompetitive. While the number of settlements that the FTC views as suspect has declined in recent years, such cases continue to occur—and the potential impact on drug pricing can be significant, particularly for high-price and/or high-volume drugs. Proposed solutions require an understanding of the unintended effects of the Hatch-Waxman Act that shape the settlements.

■ Patent Adjudication And “First Generic” Incentives

The Hatch-Waxman Act establishes a special process for adjudicating patent rights asserted by innovator pharmaceutical companies over their brands. Inno-

“The law includes an incentive for generic companies to challenge patents.”

vator companies must publicly identify patents that they believe preclude generic competition. Companies filing a generic drug application (an Abbreviated New Drug Application, or ANDA) must certify whether they intend to challenge any of those patents or wait until they expire before launching their product. If an ANDA applicant challenges a patent, it states its intent to do so in its application—known as a Paragraph IV certification, after the subsection of the law establishing the process. Assuming that the innovator files suit to protect its patent from the challenger, the Food and Drug Administration (FDA) is prohibited from approving the generic application for thirty months unless a court rules in favor of the generic earlier than that.

The law also includes an incentive for generic com-

panies to challenge patents: six months of market exclusivity granted to “first generics”—meaning that no other generic application for the same drug can be approved for that period of time. Without the incentive, generic companies may be less likely to take on the expense of litigation to challenge a patent, since a victory in court could open up the market to multiple competitors simultaneously.

Over time, first-generic exclusivity became a critical component of the profitability of the generic sector. A first generic is often priced at a relatively modest discount to the brand; once multiple generics enter the market, [pricing erodes](#) rapidly to as much as 90 percent less than the brand, according to an FTC working paper. As a result, even very large generic companies depend on short-periods of high profit margins from a handful of first generics with market exclusivity.

The Hatch-Waxman Act also defined the filing of a generic drug application as an act of patent infringement. This allows the innovator to initiate litigation to protect its patent even before a generic firm has FDA approval to sell a competing product. Normally, patent litigation can be brought only when a competitor is actually selling a potentially infringing product. For the first decade after the Hatch-Waxman Act, the FDA interpreted the generic incentive as applying to the first company to “successfully defend” a patent infringement case. Thus, if more than one generic firm challenged the patents for a given brand, the FDA would wait until one applicant won its case, and that applicant would be awarded the six-month first-generic exclusivity upon approval.

That changed in 1997, when a federal court ruled in *Mova v. Shalala* that the FDA policy contradicted the plain reading of the statute, which says that the six-month exclusivity is awarded to the first applicant to file an ANDA challenging an innovator’s patents. That ruling was upheld [on appeal](#) in 1998, and questions about pay-for-delay settlements began (Exhibit 1).

■ FTC Brings Cases Asserting Anti-Competitive Behavior

The *Mova* ruling changed the dynamics of generic patent settlements dramatically. By law, the FDA cannot approve any subsequent applicants until the first-

to-file applicant's six-month exclusivity expires. So if the first applicant agrees to settle litigation with a negotiated future launch date, that settlement blocks all generic applicants until six months after that date.

Those circumstances raised questions about the terms of many brand/generic settlements. The FTC began to investigate settlements where it believed the innovator and first-to-file challenger might, in effect, be colluding to delay the onset of generic competition. Instead of using the litigation to clear out invalid or inapplicable patents, the FTC believed that the settling parties might agree to preserve most of the claimed patent life—and share the increased profits that the brand-name product collects in the meantime.

The FTC routinely challenges business agreements between competing firms that it believes are anti-competitive. However, courts generally encourage settlements that “split the difference” in patent cases—a legitimate (not anti-competitive) reason for brand and generic firms to compromise on the launch date for the challenger. In building antitrust cases, the FTC explicitly flagged “reverse payments” as a marker of anti-competitive intent. Such payments could be overt cash transfers or side agreements for product licensing or other less direct compensation. The FTC

argued that the flow of money was backwards; in most patent cases, the innovator collects damages or compensation from the alleged infringer—not the other way around.

The FTC brought several antitrust cases starting in 2000 challenging settlements that involved reverse payments and had some success in opening up competition for specific products. The agency also persuaded Congress to include a provision in the Medicare Modernization Act of 2003 requiring that all brand/generic patent settlements be submitted to the FTC for review, giving the agency an opportunity to challenge settlements that it deemed anti-competitive.

However, the agency ultimately failed to persuade federal courts to accept the notion that reverse payments should always be treated as evidence of anti-competitive intent, and several of FTC's early victories were overturned on appeal. In 2013 the issue went to the Supreme Court (*FTC v. Actavis*), which declined to define reverse payments as per se anti-competitive. However, the Court also rejected arguments from the pharmaceutical industry that settlements allowing generic entry before expiration of the patent(s) at issue should be assumed to be pro-competitive. Instead, the Court determined that settlements

EXHIBIT 1

“Pay For Delay”—A Timeline

1984	Hatch-Waxman generic drug law enacted.
1997	<i>Mova v. Shalala</i> decision determines that the first generic applicant to challenge an innovator patent has rights to six months of market exclusivity—and the FDA is prohibited from approving other generic applicants even if they win patent challenges that would allow them to come to market sooner.
1999	FTC investigation of potential pay-for-delay agreements becomes public.
2000	The FTC settles first antitrust case on pay-for-delay grounds, involving Abbott and Geneva Hytrin patent dispute.
2003	Medicare Modernization Act requires disclosure of pharmaceutical patent settlements to the FTC for antitrust review.
2005	Appellate courts overrule the FTC in three cases, declare that reverse payments are not inherently anti-competitive; per FTC testimony, the FTC sees reverse payment settlements resume after five-year hiatus.
2013	Supreme Court rules in <i>FTC v. Actavis</i> that reverse payment cases may be challenged using a “rule of reason” analysis but does not define payments as per se evidence of antitrust violation.
2015	The FTC reaches \$1.2 billion settlement with Cephalon resolving pay-for-delay investigation.
2017	The FTC announces new pay-for-delay cases involving settlements for two different brand-name drugs.

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should be subject to a “rule of reason” test that allows antitrust challenges to continue. Since then, the FTC has concluded a number of additional settlements involving pay-for-delay cases—including a \$1.2 billion recovery from brand company Cephalon in 2015.

brought in 2000—as the industry was put on notice that the FTC viewed such payments as inherently anti-competitive. Reverse payments resumed and accelerated after appellate courts overruled the FTC on that point in 2005.

■ The Future Of Pay-For-Delay Policy And Drug Pricing

A number of important issues will play into the future impact of patent settlements and pay for delay on drug prices.

STAKEHOLDER ALIGNMENT

On most issues involving interpretation of the Hatch-Waxman Act, the brand and generic industry segments are on opposite sides. However, they are united in their view that patent settlements should be seen as pro-consumer, or at least not inherently anti-competitive.

A PRECEDENT FOR ACTION

According to the FTC, a “bright line” for antitrust enforcement worked in the past. The agency [has noted](#) that settlements involving reverse payments virtually disappeared for five years after the first cases were

PAY-FOR-DELAY IN DECLINE

According to the FTC’s most recent (2016) staff [report](#) on the issue, suspect agreements have fallen in absolute terms and as a percentage of all patent settlements reviewed by the agency since the 2013 Supreme Court decision in *FTC v. Actavis*. However, the FTC continues to identify settlements that it believes are anti-competitive, with new cases [announced](#) in 2017.

POTENTIAL SAVINGS

Legislation to support the FTC’s approach would result in modest but meaningful savings for drug purchasers. Legislation setting a standard that reverse payments are presumed anti-competitive would save more than \$2.4 billion in federal spending over ten years, according to the [Congressional Budget Office score](#) of a bill proposed by Sen. Amy Klobuchar (D-MN) in 2015. There would also be savings for consumers and private insurers.

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Cite as: “Health Policy Brief: Patent Settlements,” *Health Affairs*, July 21, 2017. DOI: 10.1377/hpb20175

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MEDICARE PART B

The Medicare Part B “buy and bill” payment structure for physician-administered drugs also influences private-sector prices.

Medicare pays for prescription drugs administered in physicians’ offices and hospital outpatient clinics as part of Part B coverage of physician services. Total Part B spending on drugs is small (\$24.6 billion in 2015), relative to Part B spending overall (\$279 billion in 2015). However, it is an important segment of the market for cancer, ophthalmic, and rheumatology drugs, and the unique Part B payment system—in which physicians purchase the drugs and are reimbursed by Medicare—helps determine pricing strategies for those products in private markets as well. Part B is also the only segment of Medicare in which federal payment is tied directly to individual drug product prices. It is, therefore, a likely area for potential reforms to enhance competition or negotiate lower prices for specific drugs.

Background

Part B, the medical component of Medicare, provides payments to physicians and hospital clinics for outpatient services. That reimbursement includes payments for physician-administered drugs (typically intravenous infusions). Part B drug expenditures were \$24.6 billion in 2015—less than 10 percent of total Part B expenditures of \$279 billion and significantly lower than Part D “retail” prescription drug spending under Medicare Part D (\$137.4 billion in 2015).

However, Part B is an important segment for several specific classes of medicines, most notably cancer, ophthalmic, and rheumatology therapies. In those markets, Part B program dynamics often influence the manufacturers’ overall pricing strategy; prices set for the government program extend to the commercial market pricing patterns, as described below. That, in turn, means that there are formidable constituencies engaged in any potential changes to the Part B program, including the medical specialty groups that use those classes of drugs.

The Part B program stands out in drug pricing discussions for several reasons. First, Part B drug expenditures have grown faster than the rest of Medicare for much of the past two decades. From 2010 to 2014 Part B grew at an annual rate over 8 percent, while total Medicare expenditures grew at just over 4 percent.

Second, a relatively small number of high-price drugs generate most of the program costs. In 2013 the program spent \$9.4 billion (47 percent of total Part B

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spending) on the top ten drugs. The nearly 600 additional covered drugs contribute minimally to total cost because of low prices or limited use.

Third, patients are responsible for a 20 percent coinsurance for Part B drugs, giving them a significant out-of-pocket stake in the program.

“There are formidable constituencies engaged in any potential changes to the Part B program.”

Finally, the congressionally mandated reimbursement formula (average sales price plus a 6 percent handling fee, as described below) favors higher-price products. Because the handling fee is a percentage, it increases with the price of the drug, which encourages physicians to use more costly therapies and manufacturers to set higher prices to attract providers to their products.

Part B is also a rare case in which Medicare policy makers can address individual drug costs directly, since payment is tied to each specific prescription. In contrast, in the Medicare hospital benefit (Part A), drug payments are included in broader reimbursements for inpatient stays. Under the Part D retail benefit, Medicare pays insurance companies a fixed amount for all necessary drugs for covered beneficiaries; there is no direct payment for specific drugs. These factors make Part B fertile ground for testing approaches to control prescription drug spending.

■ Part B: What You Need To Know

The Medicare Part B payment system includes several unique features that distinguish the program from many public and private models of prescription drug coverage.

“BUY-AND-BILL” MODEL

Part B uses a reimbursement or buy-and-bill model, meaning that providers purchase the drug first, then

bill for it after it is administered. Given that some Part B drugs are quite expensive, the certainty of the reimbursement and the attractive add-on handling fee (described below) are important considerations for providers.

THE “SPREAD”

When the program began, the government payment for Part B drugs was tied to a published “list” price, but most providers actually paid much less than that amount when they bought the drugs. Providers came to depend on the “spread” between the purchase price and the Part B payment rate as a source of revenue.

Over the past two decades, four congressional and administrative changes to the reimbursement formula have focused on setting the product cost component of the reimbursement closer to actual market prices (Exhibit 1). Those changes have reduced, but not eliminated, the spread.

ASP + 6 PERCENT

The current payment formula was set in 2003 as part of the Medicare Modernization Act. It ties payment to the average sales price (ASP), a manufacturer-reported average of actual market prices for a given product, after rebates, discounts, and other price concessions. The reimbursement is set at 106 percent of ASP to account for variability in actual prices available to providers and to include payment for providers’ handling costs.

While the statutory payment rate remains ASP + 6 percent, the sequestration provisions of the Budget Control Act of 2011 mandate a 2 percent reduction across Medicare expenditures. Because the sequester does not affect the patient copay component of reimbursement, the 2 percent cut means that the effective payment rate for Part B is now ASP + 4.3 percent.

INCENTIVES AT CROSS PURPOSES

Policy makers intended the switch to ASP-based reimbursement to encourage cost-conscious purchasing and therefore price reductions. Providers have an incentive to seek discounts as far below the Part B payment rate as possible. If manufacturers give better prices, the ASP will decline over time, and Medicare reimbursement will decline as well. However, the 6 percent add-on operates in the opposite direction,

encouraging providers to prescribe products with a higher ASP to capture a larger “spread.”

and members of Congress and was not implemented. However, it included several elements that policy makers might revisit. These include:

The Future Of Medicare Part B

Several important issues will play into the future trajectory of drug spending under Part B

REVISITING A PROPOSED DEMONSTRATION

In 2016 the Centers for Medicare and Medicaid Services (CMS) proposed a Part B demonstration program based on a June 2015 report from the Medicare Payment Advisory Commission (MedPAC). The proposal drew widespread objections from providers

- **Using a flat fee rather than a percentage add-on to ASP:** The demonstration would have changed the reimbursement formula from ASP + 6 percent to ASP + 2.5 percent, plus a flat fee of \$16.80 per prescription. The fee was intended to ensure that average reimbursements across Part B would stay the same, while reducing incentives for providers to choose a drug with a higher ASP versus a lower one. In fact, the flat fee would make very-low-price drugs attractive, since the add-on fee might be more than double the cost of the drug.

EXHIBIT 1

Part B Reimbursement Formula: A Short History

Date	Reimbursement Formula	Comments
1992 (Physician Fee Schedule for 1992)	100% Average Wholesale Price (AWP) —a published suggested wholesale price or “list” price. Estimated Acquisition Cost (EAC) used for high-volume, low-cost items.	CMS initially proposed that reimbursement be set at 85% of a national AWP but backed off when the agency “received many comments, primarily from oncologists, indicating that an 85 percent standard was inappropriate.”
1997 (Balanced Budget Act of 1997)	95% AWP for single-source products; lower of 95% of median AWP for generics in multisource category or 95% of AWP for lowest brand-name product.	Several reports from the HHS Office of Inspector General in 1996 and 1997 found that 100% of AWP bore “little or no resemblance to actual wholesale prices.”
2005 (Medicare Modernization Act of 2003)	106% Average Sales Price (ASP) , calculated by CMS from quarterly sales data provide by manufacturers from their sales to all purchasers in the US. ASP is net of any price concessions such as volume, prompt-pay, and cash discounts; free goods contingent on purchase requirements; chargebacks; and rebates other than those obtained by the Medicaid drug rebate program.	Six percent add-on payment created to help cover the overhead costs associated with the drug and differences in acquisition costs. A 2010 analysis of the new rate for reimbursement of chemotherapy drugs versus a transition rate in 2004 found that “the new payment system set chemotherapy reimbursements at 1.06 times the average costs of the drugs. This rate represented a notable decline from the 2004 weighted average payment-to-cost ratio of 1.22.”
2013 (Budget Control Act of 2011; Sequester, March 2013)	104.3% ASP —net effect of the 2% sequester reduction for Medicare payments is reduced to 1.6% because patient copays are not reduced.	“For example, for a \$100 charge where the patient co-pay is 20 percent or \$20, sequestration reduces the \$80 Medicare payment to \$78.40. Assuming the provider receives the full co-pay, total reimbursement drops to \$98.40, not \$98.00. The net effect in this example is a 1.6 percent reduction.” Explanation by Alex Brill (American Enterprise Institute) and Brett Leitner (Hooper Lundy & Bookman), June 11, 2013.
2016 (CMS proposed demonstration project—not implemented)	102.5% ASP plus \$16.80 per day of drug use.	CMS calculated the two-piece reimbursement formula to create the same aggregate spending as the current 1.06% ASP formula across the full line of Part B drugs. CMS describes the new formula as being more generous for lower-price items than higher-priced ones.

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- **Outcome-based payments:** A second phase of the demonstration would have tied payment to outcomes associated with use of a drug, or to a third-party assessment of a given therapy's value. The proposal never got far enough beyond objections to the first step of the demonstration (the rate change) to generate substantial discussion.
- **Reference pricing:** The demonstration would also have applied reference pricing in classes where there are two or more similar options available. The formula would tie reimbursement to the lowest-cost option, the average price of all the options, or the price of a specific therapy deemed most cost-effective.

MERGING PARTS B AND D

The federal government's multiple modifications to the reimbursement formula indicate its intent to bring Medicare payment rates closer to what the broader market pays for physician-administered drugs. These refinements have been necessary because the private sector adjusts quickly to new reimbursement formulas, continuing to make the buy-and-bill system attractive for manufacturers and physicians.

These dynamics suggest a different solution: folding Part B drugs into Part D, Medicare's program for outpatient drugs. Doing so would shift payment controls onto private insurers with cost-control mechanisms such as formularies, which are not used in Part B. At a minimum, that change would eliminate any artificial incentives at play in the selection of therapies in categories where oral medicines covered by Part D are available as alternatives to injectable/infusion therapies covered by Part B.

Such a proposal, however, would need to take into account the potential impact on provider payments

(such as the loss of the spread) and on beneficiary cost sharing. Part D plans can impose relatively high copayment levels; in some cases, that might mean exposing beneficiaries to more than the 20 percent coinsurance required under Part B.

COMPETITIVE BIDDING

One of the abandoned pieces of the 2003 Medicare Modernization Act was the establishment of a competitive bidding system to inject market competition into Part B. [MedPAC has suggested](#) restructuring the previously proposed Competitive Acquisition Program (CAP) as follows: (1) Empowering contracted private-sector vendors to use selective formularies to negotiate discounts from manufacturers—and share associated savings among beneficiaries, physicians, and the vendor; and (2) encouraging physicians' enrollment in CAP by removing the 6 percent handling charge from the existing buy-and-bill program. While less ambitious than abandoning buy-and-bill completely or folding Part B into Part D, this approach faces many challenges, including strong support from physicians and manufacturers for the 6 percent handling charge.

BUNDLED PAYMENT

Over the years some Part B drugs have moved from the standard reimbursement model to being included as part of bundled price-for-therapy approaches. Bundling—the model used with kidney dialysis as well as CMS's Bundled Payments for Care Improvement initiative—injects competition among all the components of care related to a procedure or episode: drugs, physician services, and any related treatments.

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Cite as: "Health Policy Brief: Medicare Part B," *Health Affairs*, August 10, 2017. DOI: 10.1377/hpb20176

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MEDICARE PART D

Medicare Part D covers retail prescription drugs for Medicare beneficiaries through unique, stand-alone drug insurance plans.

In its first decade, Medicare Part D has been popular with beneficiaries, providing important benefits to more than forty million people at lower costs than projected. However, recent trends suggesting that spending growth is exceeding that of Medicare overall have revived calls to apply the buying power of Medicare more directly to controlling prescription drug prices.

Background

The Medicare program was enacted in 1965 to provide subsidized health coverage for the elderly and disabled. The program initially covered hospital stays (Part A) and physician office visits (Part B), and Medicare paid for the prescription drugs used in those settings. The program did not, however, cover retail prescription drugs that consumers purchase from pharmacies—by far the largest volume of prescription drug use then and now.

In 2003 the Medicare Modernization Act created a drug benefit for seniors called Part D. The benefit went into effect on January 1, 2006. A decade later nearly forty-two million people are enrolled in Part D, and the program pays for almost two billion prescriptions annually, representing nearly \$90 billion in spending. Part D is the largest federal program that pays for prescription drugs.

Part D is popular with Medicare beneficiaries, and its costs have been below initial projections. Recently, however, Part D spending has grown faster than the rest of Medicare, and the Medicare Trustees predict that trend to continue for the next decade. In addition, the unique benefit structure of Part D can expose beneficiaries to high costs

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Part D: What You Need To Know

The Medicare Part D prescription drug benefit includes several features that distinguish it from other public and private models of prescription drug coverage.

STAND-ALONE DRUG INSURANCE

The Part D program operates using an insurance model—but one that is designed exclusively to cover prescription drug costs. That differs from most

health insurance plans in the private sector and from the Medicare Advantage (MA) program, which typically cover the full range of medical spending, including hospitals, physician visits, and prescription drugs. The Part D program operates both as a stand-alone benefit and as an add-on to the MA program; so-called Medicare Advantage–Prescription Drug (MA-PD) plans operate like commercial insurance policies in covering the full range of medical spending.

“The leverage of any individual plan is limited by the size of its enrollee base.”

In contrast, stand-alone Part D plans cover only drugs and so have some unique features. Beneficiaries’ costs for stand-alone Part D plans are directly related to the expected prescription drug spending in the population, so annual premiums and cost sharing generally increase in line with drug spending trends. In addition, stand-alone Part D plans do not have any exposure to increased health care costs outside of the retail drug sector—nor do they benefit from any potential offsetting savings if higher use of drugs reduces other costs, such as hospitalization.

BENEFIT DESIGN/THE “DONUT HOLE”

While Part D’s drugs-only focus is unique, the basic operation of a Part D plan relies on tools used widely by private insurers. Enrollees pay a monthly premium. There is usually a deductible, and then enrollees pay a share of the cost of their prescriptions, with the plan paying the rest. Plans use formularies, almost always with tiers that assign lower patient cost-sharing amounts to preferred drugs.

Initially, beneficiary spending is supposed to represent 25 percent of drug costs, with the plan covering the other 75 percent. As in many insurance products, there are “catastrophic coverage” protections for beneficiaries with high out-of-pocket expenses (above \$4,950 in 2017). During the catastrophic phase of the benefit, enrollees pay 5 percent of the cost of prescriptions.

Originally, the program included a gap between the initial insurance coverage and the trigger point for catastrophic coverage, universally known as the “donut hole.” The Affordable Care Act of 2010 “filled in” the donut hole: Manufacturers of brand-name drugs were required to provide a 50 percent discount on drugs purchased during that phase of the benefit, with the federal government covering an additional portion of the cost. The federal cost sharing is phasing in, and as of 2020 the basic formula of a 25 percent/75 percent split in costs will apply all the way up to the catastrophic cap.

PRICE NEGOTIATION AND NONINTERFERENCE

The Part D program design assumes that private insurers offering drug coverage have an incentive to negotiate the lowest possible price for drugs to provide a competitively priced plan to attract enrollees and maximize profits. However, the leverage of any individual plan is limited by the size of its enrollee base. While some large insurers have a national Part D presence, no single entity represents more than 21 percent of Part D lives.

By law, the Medicare program itself is prohibited from “interfering” in price negotiations between plans and manufacturers. That limits the ability to pool the entire Medicare population to improve negotiating leverage.

LOW-INCOME SUBSIDIES

Federal subsidies for low-income people are built into Medicare Part D, which immediately replaced Medicaid as the source of drug coverage for “dual eligibles”—people who qualify for both Medicaid and Medicare. Low-income Medicare beneficiaries receive sliding-scale, income-based subsidies that limit Part D cost-sharing requirements. Subsidies also greatly limit these beneficiaries’ price-sensitivity when choosing prescriptions.

The transfer of dual eligibles from Medicaid to Medicare Part D eliminated manufacturers’ obligation to pay [Medicaid rebates](#) on those patients’ prescriptions. For certain medicines at the time (for example, antipsychotics), the dual eligibles were a large portion of sales, and relief from Medicaid rebates meant higher profits on those products.

FORMULARY OVERSIGHT

In overseeing Part D, the Centers for Medicare and Medicaid Services (CMS) seeks to prevent drug insurers from enrolling only healthy beneficiaries or discouraging use of medically necessary drugs to lower costs. For example, CMS requires Part D plans to cover at least two different drugs in each therapeutic class and all drugs in six “protected classes,” including drugs for cancer, HIV, depression, schizophrenia, transplants, and epilepsy.

Key Questions For Drug Pricing

There are several outstanding questions about how the Part D program could be improved to control drug costs or lower beneficiary spending.

IMPACT OF HIGH-PRICE DRUGS

Part D includes a government-paid subsidy to protect plans from significant losses resulting from outlier enrollees. The result is that plans are exposed to only 15 percent of the cost of drugs over the catastrophic limit, with the beneficiary paying 5 percent and the federal subsidy (known as reinsurance) paying the remaining 80 percent.

As noted, the catastrophic limit is currently \$4,950 of beneficiary spending, implying about \$7,500 in total drug costs. Because many prescription drugs now cost significantly more than \$7,500 annually, the reinsurance portion of Part D has become the **fastest-growing cost** in the program.

In addition, while the share of expenses paid by beneficiaries is only 5 percent during the catastrophic phase of the benefit, there is no cap on total annual out-of-pocket spending, so individual costs can be quite high for enrollees with very high prescription costs. Among other factors, high beneficiary costs have led to proposals to change the catastrophic benefit design to increase plans’ exposure to those expenses, encouraging them to negotiate more aggressively for savings on high-price drugs.

PLANS’ MANAGEMENT OF FORMULARIES

In 2014 CMS proposed changing the six-protected-class rule to promote price competition in several of

the categories, estimating a savings of \$720 million over five years. However, CMS dropped the proposal in response to negative feedback, particularly from patient organizations, who were more concerned about plans **denying coverage of appropriate medicine** than about the impact of higher prices.

THE RIGHT USE OF REBATES

In Medicare Part D, as in other drug markets, some stakeholders are concerned about the difference between list (or retail) prices and net prices after manufacturer rebates to purchasers. Manufacturers argue that consumers are often charged cost-sharing amounts based on a list price that does not reflect discounts and rebates negotiated with the plan. Those amounts are carefully tracked and accounted for in the insurer’s bid to participate in Part D, but they are often applied to lower the monthly premium, not the amount paid by individual beneficiaries at the point of sale. In its approval of individual bids, CMS could encourage different approaches to applying rebate dollars. The question is whether rebates should be used to lower the price paid by individuals who need a particular drug or to lower the premiums paid by all beneficiaries who buy the insurance product.

MEDICAID-LEVEL REBATES

The transfer of the dual-eligible population to Medicare Part D was a significant benefit to manufacturers in 2006. The Health and Human Services Inspector General **estimated** in 2012 that the average Part D rebate among the 200 top-selling drugs was 15 percent, compared to 47 percent in Medicaid. The main reason for the difference is that Medicaid rebates are adjusted for inflation, while Part D plans (like other private purchasers) negotiate rebates off of current list prices. Those findings led to proposals to impose Medicaid-level rebates on Part D for beneficiaries receiving low-income subsidies, including dual eligibles. According to the **Congressional Budget Office (CBO)**, that proposal would save \$145 billion in federal spending over ten years.

SHOULD MEDICARE NEGOTIATE PRICES?

The call for Medicare drug price negotiation is almost as old as the Part D program itself and tied to the “noninterference” clause. However, the CBO **found**

that government negotiation would offer no inherent savings to the program. That is largely because there are no structures in place to allow Medicare to exclude drugs from the entire Part D program if a manufacturer refuses to negotiate a price. Moreover, the CBO concluded that private plans are already reasonably successful in driving price concessions, given that they can exclude drugs from their own formularies when there are multiple entrants in a given class. The CBO's analysis also acknowledges that the noninterference clause doesn't eliminate the federal government's ability to jawbone manufacturers into reducing prices case by case.

Recent work by policy development groups has fleshed out proposed price negotiation systems, including calls for a binding arbitration process that would involve third-party cost-effectiveness reviews to define a "fair" price. It is not clear whether those proposals would, in fact, deliver savings.

Key Terms

- **"Noninterference" clause:** A provision in the Medicare Modernization Act states that the Department of Health and Human Services "may not interfere with the negotiations between drug manufacturers and pharmacies and Prescription Drug Plan sponsors; and may not require a particular formulary or institute a price structure for the reimbursement of covered Part D drugs."
- **Dual eligible:** People who qualify for both Medicare (because of age or disability status) and Medicaid (based on income). Prior to Part D, dual-eligible beneficiaries had drug coverage through the Medicaid program. They are now enrolled in Part D.
- **Protected classes:** Informal shorthand for six therapeutic categories for which CMS determined that Part D plans must cover each different drug approved for that use. (CMS refers to them as the six "classes of clinical concern.")

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Cite as: "Health Policy Brief: Medicare Part D," *Health Affairs*, August 10, 2017. DOI: 10.1377/hpb20177

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MEDICAID BEST PRICE

The Medicaid best price policy requires drug manufacturers to give Medicaid programs the best price among nearly all purchasers.

Medicaid “best price” was a legislated policy solution enacted over twenty-five years ago to address high drug costs and make Medicaid drug spending more manageable for states. Under this policy, a drug manufacturer must offer state Medicaid programs the best price given to any other purchaser (with a few exceptions) with a mandatory rebate of 23.1 percent off the list price. Medicaid programs must, in turn, cover all of the manufacturer’s prescription drugs, with few exceptions. States, payers, and manufacturers are considering whether the Medicaid rebate and best price system is still effective policy or whether the arrangement unintentionally inhibits new ways to lower drug costs and improve access to therapies.

Background

In 1989 the Senate Special Committee on Aging issued a milestone [report](#) on prescription drug prices. The report stated, “Rising drug prices, particularly the high prices of new drugs, are driving State Medicaid program costs and projected Medicare drug benefit expenditures to unsustainable levels, causing the Congress to consider reducing benefits to the elderly and poor, and forcing State legislatures to choose between funding drug benefits or other health care needs of the elderly and poor.” The committee investigation was one of several efforts that led to enactment of the Medicaid drug rebate program as part of the Omnibus Budget Reconciliation Act of 1990.

The Medicaid drug rebate program requires a drug manufacturer to enter into a national agreement with the Department of Health and Human Services whereby states get the so-called best price offered to any purchaser (there are exceptions) in exchange for Medicaid coverage of essentially all of the manufacturer’s drugs. Manufacturers must also provide rebates to certain safety-net providers under the federal [340B drug pricing program](#) and to the [Department of Veterans Affairs](#) as part of the agreement.

Program participation by drug manufacturers is essentially mandatory; companies declining to participate are excluded from all federal programs, including Medicare. Approximately [600 manufacturers](#) have entered into rebate agreements. Medicaid beneficiaries have broad access to medications with minimal out-of-pocket expenses, and states have recouped financial returns in the form

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of rebate streams from manufacturers. The federal government shares in the Medicaid rebates as well. The weakness of the program, however, has been its failure to lower the growth rate of Medicaid drug spending over time, given that manufacturers control launch prices of new drugs and can account for rebates in the prices of new products.

“Companies declining to participate are excluded from all federal programs.”

The combination of Medicaid expansion under the Affordable Care Act (ACA) and a recent increase in new drug approvals, many of which have high launch prices, have coalesced to increase overall Medicaid prescription drug spending. Medicaid spent approximately **\$57 billion** on prescription drugs in 2015 (the most recent year for which there are full data), compared to **\$42 billion** in 2014.

The issue was brought to a head with the market entry of high-cost curative hepatitis C drugs in 2014. With large numbers of Medicaid recipients eligible for these medications and state requirements to cover the drugs as part of the drug rebate program, the high prices put many state budgets in crisis. Given the requirement for most states to balance budgets annually, some states had to choose between treating all eligible patients with a curative therapy or funding other fundamental state programs outside of health care.

■ Medicaid Best Price: What You Need To Know

Certain features of the Medicaid best price policy are critical to understanding its impact on prices in Medicaid and elsewhere.

THE REBATE FORMULA

The “best price” rebate formula applies to sole-source innovator drugs distributed to Medicaid beneficiaries. The best price must be reported to the Centers

for Medicare and Medicaid Services. The statutory rebate formula takes into account three factors: (1) the Average Manufacturer Price (AMP), or list price, of the drug, which is intended to account for different discounts and price concessions for other purchasers; (2) either a minimum rebate of 23.1 percent off of AMP or the “best price” offered to any other private or public purchaser (with a few exceptions—see below) if such a purchaser receives more than the minimum discount; and (3) an adjustment if the drug price rises faster than inflation. For older drugs, the inflation component is often a significant factor in the size of the rebate.

There are different minimum rebates for certain drug categories. For example, blood clotting factors and drugs approved exclusively for pediatric populations use a minimum rebate of 17.1 percent off AMP per unit. Generic drugs have a separate rebate formula, including a minimum rebate of 13 percent and an inflation adjustment similar to the one noted above, but no “best price” component.

Each state Medicaid program tracks drugs purchased for recipients and submits quarterly invoices to manufacturers for rebates. Manufacturers must update AMP and inflation calculations and ensure that they pay the correct rebate. That builds in some lag time between actual market prices and Medicaid rebates.

EXEMPTIONS FROM BEST PRICE

There are several excluded programs that do not trigger the “best price” guarantee for Medicaid. These include federal health systems such as the Department of Veterans Affairs and the Department of Defense and also prices negotiated by private plans operating Medicare Part D plans. Such programs can receive a lower price than Medicaid for a given drug.

ACA CHANGES TO MEDICAID REBATE

The ACA made several changes to the Medicaid rebate program. The biggest impact was the change in the minimum rebate from 15.1 percent to 23.1 percent. The law also defined the AMP more broadly, leading to some adjustments in the baseline price from which rebate percentages are calculated. A new rebate was added for product-line extensions, **defined in the law and by clarifying regulation**. In addi-

tion, the law capped rebates at 100 percent of AMP. Unlike other statutory changes, this change reduced manufacturer rebates, as some products with significant price increases over time actually owed a rebate of more than 100 percent, because of the inflation adjustment built into the rebate formula. In other words, states were ultimately recouping more than the cost of the medicine in the form of a rebate.

REBATES AS A REVENUE STREAM FOR STATES

The time lag built into the program tends to encourage states to treat rebates as a stand-alone income line in the budget, instead of looking at total Medicaid drug spending. The amount is significant: In fiscal year 2014, Medicaid programs spent \$42 billion on prescription drugs and collected about \$20 billion in rebates.

THE “BEST PRICE” FLOOR

One ripple effect of guaranteeing the best price for Medicaid is that it weakens the leverage of private commercial payers and pharmacy benefit managers (PBMs) in negotiations with manufacturers, in effect setting a floor under prices. Private payers argue that they would be able to negotiate even lower prices for patients if manufacturers were not obliged to offer the same price to all fifty state Medicaid programs. Best price is also confidential by law, so manufacturers could use that argument to deny a discount below the 23.1 percent minimum, even if they did in fact provide better pricing to other customers (although misreporting best price or otherwise violating the rules for calculating Medicaid rebates can be prosecuted as a violation of the False Claims Act).

■ The Future Of Medicaid Rebates And Best Price

Several important issues will play into the future impact of rebates and best price on Medicaid drug spending.

IMPACT ON OUTCOMES-BASED PURCHASING

Policy experts, lawmakers, drug developers, and payers are generally united in their desire to explore the potential of outcomes-based drug purchasing

models (also called “value-based” purchasing models). Under such models, the payer and manufacturer agree upon assumptions about a drug’s expected improvement in outcomes for the population. If the drug fails to perform as expected, the manufacturer must pay a rebate to the purchaser. However, according to a July 2016 [policy notice from CMS](#), manufacturers’ concerns over compliance with best price provisions have made some wary of entering into those agreements, which might ultimately lower the best price. In that memo, CMS says that value-based purchasing contract questions, as they relate to the best price requirement, should be taken case by case and that manufacturers should seek guidance from the agency when seeking to enter into these agreements. One interpretation of the policy notice is that manufacturers are encouraged to experiment with outcomes- or value-based models in Medicaid first, as opposed to attempting to employ the agreements in the private sector.

AN OPT-OUT FOR STATES

Some state program administrators and Medicaid managed care organizations have explored the potential benefits of a state opt-out from the Medicaid rebate program. The driving factor is the requirement that essentially all outpatient drugs from a given manufacturer must be covered by the state in exchange for the best price guarantee and rebates. For some states, the financial risk of covering all drugs, including new high-cost therapies, is not worth the benefit of the rebate. Eliminating that requirement and moving to more aggressive formulary management tools could give Medicaid programs more latitude for responding to high-price new therapies entering the market.

OTHER OPTIONS FOR STATE SAVINGS

Instead of significantly altering the best price paradigm, policy makers could dial up the minimum rebate further. The sole-source brand rebate was originally phased in from 12.5 percent in 1990, to 15.1 percent in 1995, to its current 23.1 percent. There is, in principle, no reason the minimum rebate could not be adjusted higher again.

Alternatively, policy makers could align the rebate program with potential caps on Medicaid spending, in

the context of either federal reforms to the program or states' initiatives to contain their share of costs. Some states have considered instituting a cap on Medicaid drug spending. New York, for example, recently passed legislation (Senate Bill S2007B) that sets a target cap on drug spending growth at 5 percent above inflation. If the target growth rate is exceeded, the breach triggers reviews by a drug utilization review board "for a recommendation as to whether a target supplemental Medicaid rebate should be paid by the manufacturer."

■ Key Terms

- **Best price:** According to statute, "The term 'best price' means, with respect to a single-source drug or innovator multiple-source drug of a manufacturer (including the lowest price available to any entity for any such drug of a manufacturer that is sold under a new drug application approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act), the lowest price available from the manufacturer during the rebate period to any wholesaler, retailer, provider, health maintenance organization, nonprofit entity, or governmental entity within the United States."
- **Outcomes-based or value-based drug purchasing:** Linking the purchase price of a medicine to a given clinical outcome or measure. If the drug fails to deliver on efficacy or safety metrics demonstrated in trials or other forms of real-world evidence, the manufacturer pays a rebate or other concession to the purchaser.
- **Average Manufacturer Price:** The AMP provides the baseline to determine Medicaid's federal upper limit on prices paid to pharmacies for generics. In addition, the new AMP calculation may also serve as the baseline for calculations states use to reimburse Medicaid drugs more broadly. Therefore, the rule impacts which drugs are new or exempted from a higher rebate, the calculation of prices, and the rebate amount. The January 2016 Medicaid Covered Outpatient Drug final rule revised the long-standing definition of AMP to "now mean the average price paid to the manufacturer for the drug in the United States by wholesalers for drug distribution to retail community pharmacies and retail community pharmacies that purchase drugs directly from the manufacturer."

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Cite as: "Health Policy Brief: Medicaid Best Price," *Health Affairs*, August 10, 2017. DOI: 10.1377/hpb2017.8

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VETERANS HEALTH ADMINISTRATION

The Veterans Health Administration can often obtain very favorable prices for drugs and may be a model for Medicare and others.

The Veterans Health Administration is a large integrated health care system operated by the Department of Veterans Affairs (VA). By law, the VA can buy prescription drugs at discounted prices. But it also negotiates for even deeper discounts on its national formulary. Because of the agency's ability to purchase some drugs at prices much lower than most commercial and government payers, it is often cited as a model for broader federal negotiation of drug prices—or as a benchmark for other purchasers to use in obtaining comparable pricing.

Background

Through the Veterans Health Administration, the VA offers health care services to qualified members of the military once they leave active duty. Unlike most federal prescription drug benefit programs, the VA does not simply reimburse claims filed by pharmacies or other providers. Instead, the VA is itself the provider, operating an [integrated network](#) of 168 medical centers, more than 1,000 outpatient clinics, 250 brick-and-mortar pharmacies, and seven mail-order pharmacies (which deliver about 80 percent of the program's prescriptions). The VA employs over 200,000 health care professionals, including doctors, pharmacists, and other providers.

The VA health system [covers](#) about nine million of the approximately twenty-two million veterans in the US. Of that total, 4.9 million used the VA pharmacy system in 2016. Prescription drug spending by the VA is [expected](#) to total about \$7 billion in 2017—slightly less than 10 percent of total health care spending in the system.

Like many federal programs, the VA has statutorily mandated access to favorable drug pricing. It also operates a national formulary and can exclude medications that the agency's formulary committee concludes are inappropriate for the patient population or should be subject to prior authorization. That, in turn allows, the VA to negotiate even deeper discounts in some cases, particularly when there are multiple suppliers of either the same (generic) ingredient, or a closely comparable brand medicine.

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■ The VA: What You Need To Know

The VA's ability to obtain deep discounts in some large therapeutic classes is often cited as a model for negotiating prescription drug prices in other federal programs, such as Medicare. The VA uses a mix of statutory and administrative tools to achieve its goals.

“The VA uses a mix of statutory and administrative tools to achieve its goals.”

DISCOUNTS GUARANTEED BY LAW

The 1992 Veterans Health Care Act granted the VA minimum discounts on drugs, similar to those received by Medicaid. Notably, the VA discount was enacted after the [1990 Medicaid rebate law](#), which guaranteed Medicaid a discounted price and also required manufacturers to give Medicaid the “best price” they offered. Once the Medicaid rebate law took effect, some manufacturers canceled discounts to other purchasers (including the VA) to avoid setting a best price that would also have to be offered to Medicaid.

The 1992 law set a ceiling on prices that manufacturers can charge the VA and several other federal purchasers (the Department of Defense [DoD], the Public Health Service, and the Coast Guard, collectively referred to as the “big four”). The price is based on the “non-federal Average Manufacturer Price,” or the average sales price to purchasers outside the federal government.

The VA is also entitled to a guaranteed minimum discount of 24 percent off the non-federal Average Manufacturer Price (an amount similar to the minimum discount guaranteed to Medicaid), or a lower price to match the best price provided to non-federal purchasers. As in Medicaid, the discount is adjusted to recoup inflationary price increases. Finally, unlike private purchasers, the VA is allowed to negotiate prices lower than the existing “best price”

without triggering an obligation for manufacturers to give the same price to Medicaid. In that respect, the VA has a stronger negotiating position than private purchasers have.

NATIONAL FORMULARY

For most of its history, the VA relied on formularies—lists of covered prescription drugs that are available for patients—operated by each of its separate facilities. Beginning in 1997, however, the VA established a national formulary, allowing the agency to leverage its purchasing power to obtain deeper discounts for individual therapies than any single facility might be able to obtain. The national formulary also helps ensure consistency of care across the VA system.

The national formulary is operated by the VA's Pharmacy Benefits Management (PBM) Services, which uses published policies and procedures to make decisions on which drugs to include in or exclude from the formulary.

PUBLISHED PRICES

The VA makes public its national formulary and a price list for most prescription drugs available in the system. Those lists serve as important benchmarks for other purchasers, although they do not necessarily reflect all negotiated discounts, since manufacturer agreements often require the final price to remain confidential.

LOW OR NO COST SHARING

Many VA beneficiaries have low or no copays or other direct costs for their care. The VA has recently shifted to a tiered drug copay system, with different cost sharing for preferred generics, nonpreferred generics, and brands. That change has lowered overall cost sharing in the system. The VA [expects to collect](#) about \$530 million in copays in 2017, down from about \$630 million the year before. It expects that amount to decline again to \$450 million in 2018, even as the number of total prescriptions dispensed in the system rises towards 250 million.

LOW PER PRESCRIPTION COSTS OVERALL

Analyses consistently [show](#) the VA having the lowest per prescription costs among all federal purchasers.

In part, that reflects the success of the national formulary process in negotiating lower prices on some top-selling brands. It is also a function of the VA's ability to encourage prescribing of lower-cost generic alternatives.

A 2013 Government Accountability Office (GAO) report [compared](#) VA and DoD prices for the most commonly used therapies in each system. Both programs have the same guaranteed discount, operate formularies, and negotiate lower prices where possible. The GAO found that the average brand-name price paid by the DoD was actually lower than the VA average for the sample, but the VA generally obtained lower prices on generic drugs, resulting in a lower average cost per prescription. In other words, the VA's ability to negotiate lower prices is not necessarily the most important reason it is able to keep drug costs down: Instead, it is the VA's ability to ensure that physicians prescribe the most cost-effective medications more frequently.

Among other tools, the PBM Services group relies on an "academic detailing" program, in which a team of VA pharmacists develops prescriber education programs to promote guidelines on cost-effective use of medicines. This is a prominent example of applying the traditional pharmaceutical sales force detailing model to the goals of a payer or health system, rather than to increasing the prescribing of a specific brand.

The success of that approach was highlighted in a 2015 McKinsey [review](#) required by the Veterans Access, Choice, and Accountability Act of 2014. The report found that "VA performs well on the key dimensions of purchasing, distribution, and use of pharmaceuticals" and that "all physicians and pharmacists interviewed believed the VA formulary helps guide good clinical decision-making around prescribing, and they expressed strong buy-in to the formulary decision-making process."

■ Key Questions For Drug Pricing

There are several outstanding questions about how the VA does or could affect drug prices for other purchasers.

THE VA AS A MODEL FOR MEDICARE

The call for Medicare drug price negotiation often invokes the VA as a model to obtain lower prices. In theory, the federal government—and Medicare beneficiaries—could save significant amounts if they had access to the VA's prices for prescription drugs. However, there are obstacles to applying the VA model in Medicare. The core structural issue is that physicians, pharmacies, and other providers serving Medicare are not employed by, or otherwise organizationally part of, the Medicare program; their relationship to the program is that of an arm's-length contractor. In contrast, VA providers are part of an integrated system that both pays for and provides care to its defined population. It would be more difficult to implement a national formulary across disparate and unrelated Medicare providers than it is to implement a formulary across integrated VA providers.

Some private purchasers can replicate the VA system's level of control over its pharmaceutical program with direct ownership of facilities and employment of, or exclusive contracting with, physicians and other prescribers (for example, staff-model health maintenance organizations such as Kaiser Permanente). Medicare beneficiaries can and do enroll in capitated Medicaid Advantage plans offered by those providers.

However, the majority of Medicare beneficiaries access care using the fee-for-service side of the program and purchase stand-alone prescription drug coverage under [Part D](#). Each of those stand-alone plans already relies on formularies and negotiates with manufacturers for discounts. Replacing those different private plans' formularies with a national one would fundamentally restructure the Part D benefit, eliminating the current feature of encouraging beneficiaries to shop for plans with formularies that best match their needs. In addition, without steps to encourage or ensure that Medicare prescribers comply with a national formulary, it could be difficult to negotiate lower prices than those already obtained by private plans. Beneficiaries might also experience higher costs or barriers to care if physicians continue to prescribe off-formulary medications.

Finally, even a successful strategy to apply VA-level pricing in Medicare could have negative effects on pricing for other purchasers. In 2000 the GAO found that one likely impact of extending VA or Medicaid pricing to the Medicare population would be an increase in prices for federal and private purchasers. Citing the experience after enactment of the Medicaid rebate law, the GAO stated that manufacturers would likely cancel other federal pricing agreements wherever possible to avoid having to extend those prices to the much larger Medicare population.

OTHER WAYS TO TAP INTO VA PRICING?

A 2016 state ballot initiative in California (Proposition 61) would have directed the state to buy drugs for its employees at VA prices. Proponents of the initiative argued that it could produce significant savings from the state's annual \$3.8 billion in prescription drug spending.

Opponents (including the pharmaceutical industry) argued that its impact might instead be to cause manufacturers to cancel agreements with the VA, leading to higher prices overall. There were also questions about the enforceability of the measure. The initiative was defeated, and the actual impact of the proposed approach has yet to be tested.

Key Terms

- **Veterans Affairs (VA) Health Benefits:** In general, any member of the military having completed at least twenty-four months of active duty is eligible for comprehensive VA health benefits after leaving active duty, provided they are not dishonorably discharged. (Veterans with shorter service time are eligible if they are discharged because of disability or for other hardship reasons.) The enrollment process assigns different levels of priority to individual veterans, and aspects of the coverage (including out-of-pocket expenses for items such as prescription drugs) depend on priority status.
- **Formulary:** A list of medicines that are available within a hospital or other institution, or that are that are covered by a specific insurance policy.
- **Non-federal Average Manufacturer Price:** Defined in 38 U.S. Code Section 8126 as “the weighted average price of a single form and dosage unit of the drug that is paid by wholesalers in the United States to the manufacturer, taking into account any cash discounts or similar price reductions during that period, but not taking into account (A) any prices paid by the Federal Government; or (B) any prices found by the Secretary to be merely nominal in amount.”

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Cite as: “Health Policy Brief: Veterans Health Administration,” *Health Affairs*, August 10, 2017. DOI: 10.1377/hpb2017.9

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THE 340B DRUG DISCOUNT PROGRAM

The 340B drug discount program mandates the sale of outpatient prescription drugs to safety-net providers at reduced prices.

Facilities and programs known as 340B-eligible “covered entities” routinely provide prescription drugs regardless of a patient’s ability to pay. However, drugs purchased at 340B prices can be dispensed to insured patients, and purchasers may bill those insurers—including Medicare—at higher rates. The program has grown rapidly, and the use of the discount by a relatively small set of large public hospitals has raised questions about whether the 340B discount is having unintended ripple effects on patient care and provider markets.

Background

The 340B drug discount program is unique to the US pharmaceutical marketplace and an important topic for understanding many dynamics of drug pricing. The program, named for the legislation that created it in 1992 (section 340B of the Public Health Service Act), requires manufacturers to sell products to selected purchasers (safety-net providers and programs identified in statute) at a discounted price.

The program was designed to address an unintended consequence of the 1990 Medicaid rebate law. Before that law, many manufacturers offered discounts to safety-net providers, recognizing that they supply prescription drugs to indigent patients who often cannot pay. However, because the 1990 rebate law requires manufacturers to provide Medicaid with rebates equal to the lowest price in the market (the “best price”), pharmaceutical companies began to cancel discount agreements with other purchasers to avoid providing the same discount to the entire Medicaid market.

Section 340B requires manufacturers to sell products to a broad set of facilities and programs at a price no higher than the net price paid by Medicaid, after rebates. (Manufacturers can sell to 340B-eligible purchasers at even deeper discounts if they choose, without triggering a new Medicaid “best price.”) The discount is required for all outpatient prescription drug products—a designation that encompasses more than the traditional retail pharmacy medicines, such as infusion therapies, provided they are not part of an inpatient stay.

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The statute lists sixteen eligible purchaser groups, including federally qualified health centers, various disease-specific programs (AIDS Drug Assistance Programs, black-lung clinics, and hemophilia treatment centers), and publicly owned hospitals with a disproportionate-share hospital (DSH) percentage of at least 11.75 percent. As a group, they are referred to as “covered entities.”

“The 340B program has expanded dramatically since 1992.”

As of 2016 there were almost 35,000 individual sites registered by the Health Resources and Services Administration (HRSA) as eligible for the discount; many are affiliates of a single parent organization. According to HRSA, drug purchases at 340B prices totaled approximately \$12 billion in 2015. Assuming a 25–50 percent discount on those purchases, HRSA estimates savings of \$6 billion for covered entities. (Actual 340B prices are not available, because of their close relationship to Medicaid “best prices” and a legal prohibition against sharing Medicaid rebate calculations publicly.)

■ 340B: What You Need To Know

Several important features of the 340B program factor into debates over its role in the broader prescription drug market.

THIRD-PARTY REIMBURSEMENT

Drugs purchased under the 340B program are not exclusively for the uninsured. While the focus of the program is on entities that provide services regardless of patients’ ability to pay, 340B-eligible purchasers can and do bill third parties, including Medicare and commercial insurers. (By law, 340B-eligible purchasers cannot bill Medicaid more than the 340B price.) The ability to obtain third-party reimbursement for

drugs purchased at 340B prices is a critical component of the program for participating providers; the difference between their price and the reimbursed amount is an important source of income. It is also a factor in policy debates about the program, as the 340B discount is essentially a subsidy for safety-net providers, but one not derived directly from taxpayer funds.

RAPID EXPANSION AND CONCENTRATION

The 340B program has expanded dramatically since 1992, and—somewhat counterintuitively—the Affordable Care Act (ACA) in 2010 led to a significant increase in use of the discount, even as the population covered by insurance increased. This was due in part to deliberate expansion of the program to include new purchasers (specifically, critical access hospitals and rural treatment centers). However, a bigger impact resulted from the expansion of Medicaid: More public hospitals became 340B-eligible DSH hospitals because the number of treated Medicaid patients is a factor in the DSH calculation.

The number of DSH hospitals enrolled in 340B almost doubled from 2005 (583) to 2014 (966), according to the Medicare Payment Advisory Commission (MedPAC). As much as 70 percent of 340B purchases (by dollar value) are made by DSH hospitals, even though they represent less than half of the hospitals enrolled in the program, and a far smaller portion of the total number of covered entities.

INCREASED PROGRAM OVERSIGHT

From 1992 through 2010 the 340B program operated largely on the honor system. For manufacturers, even verifying a purchaser’s eligibility could be difficult, since there was no formal certification or listing requirement. The lack of transparency also led to concerns that discounts were being used inappropriately and that manufacturers were unfairly denying sales at 340B prices. The ACA established formal certification and audit requirements, with both purchasers and manufacturers subject to audits. Covered entities are now required to reimburse manufacturers if an audit finds inappropriate use of discounts.

UNCLEAR HRSA REGULATORY AUTHORITY

The 340B program has operated largely via direct implementation of the statute and informal communication by the HRSA Office of Pharmacy Affairs. After the ACA's enactment, HRSA began drafting formal regulations defining key aspects of the program, including how to determine who counts as a "patient" of a 340B purchaser for purposes of the discount. Before those draft regulations could be issued, however, a federal court ruled (in a case brought by the pharmaceutical industry challenging a separate 340B policy) that HRSA lacks authority to issue 340B implementing regulations, except in specific areas explicitly authorized by Congress.

In light of that ruling, HRSA abandoned the broader regulation; instead, the agency issued many of the proposed program definitions in the form of a draft [guidance](#). However, that draft was withdrawn at the beginning of the Trump Administration. The lack of formal regulatory authority for HRSA calls into question whether the agency could enforce program definitions if the guidance is finalized. That has led to calls for legislation to grant HRSA explicit authority to issue and enforce regulations governing the program.

■ Important Issues For The Future Of The 340B Program

Several unresolved issues and unanswered questions will shape the 340B program going forward.

WHO BENEFITS FROM THE DISCOUNT?

According to the Congressional Report language accompanying the 340B statute [H.R. Rep. No. 102-384(II), at 12 (1992)], the purpose of the discount is "to stretch scarce federal resources." Covered entities interpret that language as indicating that they are supposed to benefit from the ability to seek third-party reimbursement amounts significantly higher than the 340B price, to provide funding to enhance their mission. Critics argue that the program has strayed far from providing access to drugs

for safety-net providers and their patients and has instead become a new funding stream for public hospitals, including those that provide relatively limited amounts of uncompensated care.

CHANGES IN ONCOLOGY PROVIDER MARKETS

The post-ACA expansion of the 340B program has coincided with a shift in treatment patterns for oncology, from community-based private practices to hospital outpatient departments. Many community oncologists see a cause-and-effect relationship, arguing that they can't compete with the margins available to 340B-eligible hospitals, which can purchase high-price cancer therapies at deeply discounted prices. Program defenders argue that the factors driving changes in the delivery system are complex and go far beyond the single issue of 340B pricing.

POTENTIALLY INAPPROPRIATE CARE

The "spread" between the 340B price and the third-party reimbursement raises questions about inappropriate or overly intense use of medications, especially in Medicare. Arguably, 340B pricing encourages providers to choose a higher-cost agent, even when a lower-cost therapy is available, because the spread will be larger and the profit margin therefore higher. The concern exists generally in [Medicare Part B](#), but it is magnified by the size of the spread for 340B providers. Part B providers receive a payment that is 6 percent more than the national Average Sales Price (ASP). In contrast, 340B providers receive a discount of at least 23 percent off the calculated Average Manufacturer Price (AMP), an [average of 34 percent](#), and often much higher (up to 100 percent)—but the same Medicare reimbursement as other providers.

■ Key Terms

- **Covered Entities:** The catch-all term for purchasers eligible for 340B discounts. By law, there are sixteen classes of eligible purchasers, ranging from small, disease-focused providers (such as hemophilia treatment centers and black-lung clinics), to community health centers, to larger public hospital systems.
- **Ceiling Price:** The maximum price a manufacturer can charge a 340B entity for a covered drug. The [formula](#) to calculate the price is intended to match the net price paid by Medicaid after rebates.
- **Prime Vendor:** The 340B law established a prime vendor program to aggregate the buying power of the covered entities. The prime vendor negotiates discounts below the 340B price on some products, and also negotiates discounts on non-pharmacy products on behalf of covered entities. Since 2003, HRSA has contracted with a non-profit start-up, [Apexus](#), as the Prime Vendor. In addition to the purchasing function, Apexus serves as an information resource for covered entities and 340B manufacturers, and often plays a role in developing solutions for complexities in operating the program on behalf of HRSA.

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Cite as: "Health Policy Brief: The 340B Drug Discount Program," *Health Affairs*, September 14, 2017. DOI: 10.1377/hpb2017.10

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PATIENT FINANCIAL SUPPORT

Manufacturer-sponsored financial support helps patients afford medicines but may thwart payers' efforts to use preferred drugs.

Patient financial support is among the most controversial issues in the public debate over high prescription drug prices and has become even more so as prices have risen exponentially in recent years. To manage escalating drug costs, payers have accelerated the use of tools such as formularies (list of preferred and nonpreferred drugs), with access limits enforced by varying rates of out-of-pocket cost sharing for patients. Drug manufacturers, in turn, often offer or fund patient financial support as a counter-strategy against payers' efforts to restrict access to certain drugs through high cost sharing. Such programs can alleviate some out-of-pocket cost burdens for patients and address financially driven nonadherence to medications. However, payers view manufacturers' financial support as an undercutting strategy to shield patients from drug costs, thereby driving use of higher-priced therapies when lower-cost generics or preferred brand therapies are available.

Background

Patients' out-of-pocket drug cost sharing is determined by their health plan's or **pharmacy benefit manager's (PBM's) formulary**—a list of preferred and nonpreferred prescription drugs. Preferred status is based on a drug's effectiveness, price, and the level of rebate the payer receives from the manufacturer for giving the drug preference over its competitors. Generics and preferred brand drugs are generally assigned lower patient cost sharing than nonpreferred brand drugs. As drug prices have increased, so has patient cost sharing, causing some patients to stretch, forgo, or discontinue medication that is too expensive. Drug manufacturers often seek to mitigate these effects by providing or funding various forms of patient financial support.

The aim of drug manufacturers' patient financial support is to minimize or remove out-of-pocket cost sharing as an obstacle when patients choose medications, thereby keeping them on brand-name drugs for longer. However, while patients might not feel the high costs of some drugs, the health system does absorb them. As a result, these programs play an increasing role in criticism of high drug spending.

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■ Patient Financial Support: What You Need To Know

Several issues are important in understanding the relationship of manufacturer-sponsored patient financial support to drug prices in the public and private sectors.

“Manufacturers cannot provide coupons to beneficiaries of government programs.”

TYPES OF SUPPORT

Manufacturers’ patient financial support may take the form of copay coupons or patient assistance programs (PAPs), which differ in important ways. The [Government Accountability Office \(GAO\)](#) defines drug coupon programs as “those through which a drug manufacturer provides financial support directly to patients to reduce their out-of-pocket costs for drugs that the manufacturer sells.” The Health and Human Services (HHS) Office of Inspector General extends the definition to include print and electronic coupons, debit cards, and direct reimbursements. Coupons, which generally do not carry income-related eligibility restrictions, have maximum annual discounts ranging from hundreds of dollars to tens of thousands of dollars.

In contrast to coupons, PAPs “provide free or discounted drugs to patients of low income,” according to the GAO. Manufacturers may either sponsor their own PAPs, which distribute free medicines to qualified patients, or donate to independent foundations that then provide patients with financial assistance. Patients qualify for these programs on the basis of financial or medical need, or both.

A critical distinction between copay coupons and PAPs is manufacturers’ ability to influence patients’ choice of a specific drug. With copay coupons, manufacturers have direct control over the drug for which

the coupon can be used. Their control over PAPs is more limited: They influence patients’ drug choices through their own PAPs by giving away specific drugs. However, when manufacturers donate to independent charitable PAPs, they are prohibited from tying the use of those funds to any specific drug.

These dynamics relate to another important distinction between copays and PAPs: Manufacturers cannot provide coupons to beneficiaries of government programs—such as Medicare and Medicaid—while such beneficiaries can be eligible for some PAPs. Coupons are considered a direct inducement to buy a specific product, in violation of the federal anti-kickback statute in the Social Security Act. This law makes it a criminal offense to “knowingly and willfully offer, pay, solicit, or receive any remuneration to induce or reward the referral or generation of business reimbursable by any federal health care program.”

However, because manufacturers’ donations to independent charitable PAPs may not be tied to the use of a specific drug, those programs are not seen as a direct inducement. According to the [Centers for Medicare and Medicaid Services \(CMS\)](#), “PAPs can provide assistance to [Medicare] Part D enrollees and interface with Part D plans by operating ‘outside the Part D benefit’ to ensure separateness of Part D benefits and PAP assistance.” One important caveat is that aid on behalf of a PAP enrollee does not count toward that enrollee’s Medicare Part D true-out-of-pocket expenditure, which determines when a beneficiary reaches the catastrophic coverage threshold at which Medicare covers the vast majority of drug costs.

Exhibit 1 lists the types of patient financial support and indicates both the level of manufacturer control and the availability of the support to public program beneficiaries.

APPROPRIATE PAP USE

Manufacturer donations to PAPs have grown significantly over the past twenty years. A [2000 GAO report](#) found that PAPs sponsored by members of the brand pharmaceutical industry group Pharmaceutical Research and Manufacturers of America (PhRMA) provided \$500 million worth of products to 1.5 million people in 1998. By 2014, donations through

PAPs increased to \$7 billion annually, 93 percent of which was attributable to manufacturer PAPs that gave away drugs, for which they received a tax write-off. In 2017, ten of the fifteen largest US charitable foundations administer some form of PAP.

As PAPs have grown in size, relationships between the organizations and drug manufacturers have come under intensified scrutiny. Some PAPs' independence has been called into question, and there have been investigations (for example, by the Internal Revenue Service) into whether manufacturers have wrongly received tax breaks as a part of the arrangements.

IMPACT ON PATIENTS' CHOICES

From the patient's perspective, financial assistance through any avenue may come as welcome relief when a physician recommends or prescribes a specific brand-name drug with a high price tag. Drug manufacturers contend that their financial support allows doctors and patients to make the most appropriate prescribing decisions, irrespective of cost. They also argue that the support improves adherence to therapy by keeping patients on their existing medicines.

On the other hand, some stakeholders have noted that the impact of coupons on consumers' out-of-pocket expenditures is time limited (most can be used for no more than a year) and that when coupons

expire, patients may be reluctant to switch to an available lower-cost generic or preferred brand with which they might not be familiar.

IMPACT ON PRICE INCREASES

Express Scripts, a large pharmacy benefit manager strongly opposed to manufacturer-sponsored financial support, cites a report that found that during the five years following generic entry, coupons increase total drug spending by \$30-\$120 million per drug, or \$700 million to \$2.7 billion for all drugs studied, between 2007 and 2010. The study concluded that coupons "are associated with faster branded price growth," with roughly a 5 percent increase in price growth per year when the manufacturer makes coupons available. (Additional published perspective pieces and studies have been similarly critical of cost increases related to PAPs.)

Coupons have also been cited as a factor in Medicare Part B drug costs. While coupons are not permitted for Part B cost sharing, manufacturers can potentially maintain high list prices for purposes of Medicare reimbursement while offering copay coupons to privately insured patients to ensure their access. A recent GAO study estimated that for eighteen of the fifty drugs with the biggest Medicare Part B expenditures in 2013, \$205 million in copay coupons were extended to privately insured patients.

EXHIBIT 1

Types Of Drug Manufacturer Financial Support And Their Uses

	Type of assistance	Can encourage/require use of a specific drug?	Can be provided to beneficiaries of government health care programs?
Copay coupons	Print or electronic copay coupons, debit cards, and direct reimbursements to offset cost sharing	Yes	No
Manufacturer-provided patient assistance programs	Free drugs	Yes	Yes
Manufacturer donations to independent charitable patient assistance programs	Direct cash grants	No	Yes

SOURCE Prevision Policy LLC.

Open Questions For The Future Of Patient Financial Support

The landscape of manufacturer-provided patient financial support is changing rapidly. Several recent developments bear watching to see how they will affect the continued use of both coupons and PAPs.

ASSISTANCE BANNED IF GENERIC AVAILABLE

Massachusetts is the only state to ban copay assistance for brand drugs when there is a generic equivalent. In fact, until 2012 the state prohibited all copay assistance, but under pressure from drug makers, the legislature lifted the prohibition with a sunset clause: The ban would take effect again in July 2017, along with the requirement that a study be conducted to determine the impact of copay assistance. The sunset clause and the study requirement were extended to July 2019, a delay again supported by the drug industry. As a result, there are as yet no real-world data to show an impact on overall health costs in the state. The distinction between banning all patient support (as in Medicare) versus only banning coupons when there is a generic available (as in Massachusetts) makes Massachusetts a unique case.

COPAY ASSISTANCE IN THE EXCHANGES

In 2013, ahead of the kickoff of the insurance exchanges (Marketplaces) created under the Affordable Care Act, there was some controversy about whether or not manufacturers could use copay coupons in the new Marketplaces. The administration concluded that the exchange markets are governed by the rules of commercial insurance, not by those of federal health programs. As a result, HHS determined that companies could use coupon programs for people enrolled in

Marketplaces, as long as health plans accepted them. It is still unclear how coupons have played out in the exchanges. The biggest complaint from manufacturers has been reduced access to their more expensive innovative therapies—one anecdotal indicator either that there are relatively few manufacturers offering copay assistance in the exchanges or that financial support is having little impact against plans' tools to drive down costs.

NEW ANTI-KICKBACK STATUTE PROSECUTION

Federal prosecutors are increasingly looking at PAPs as relative unexplored territory in relation to the anti-kickback statute. Prosecutors have disclosed a number of investigations but have made no concrete allegations. The growth of the programs and proportional acceleration in drug sales in some cases have made PAPs a visible target for further investigation. Like False Claims Act prosecutions centered on off-label marketing or Medicaid "best price" violations, for example, the PAPs may be viewed as an attractive revenue line for prosecutors to pursue settlements under the HHS initiative to stop waste, fraud, and abuse.

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Cite as: "Health Policy Brief: Patient Financial Support," *Health Affairs*, September 14, 2017. DOI: 10.1377/hpb2017.11

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FORMULARIES

Formularies are tools used by purchasers to limit drug coverage based on favorable clinical performance and relative cost.

Formularies are lists of drug products covered by payers that distinguish between preferred or discouraged products by dividing outpatient therapies into three to five “tiers,” each with a different level of patient cost sharing. The application of formularies to drug selection is similar to the application of medical treatment guidelines (used by medical specialty groups, health care providers, and insurers) to decisions about treatment regimens. Formulary selection involves an assessment of products’ clinical performance and relative cost. Formularies convey substantial leverage to purchasers in negotiations with manufacturers. That leverage is the primary cost-control mechanism in Medicare Part D (the drug benefit portion of Medicare) and in most private insurance plans. Formularies limit coverage for drugs that the payer has determined do not show adequate clinical differentiation or benefit to justify the cost.

Background

Formularies have grown in importance as both drug-selection and cost-control tools over the past three decades. The emergence of formularies in the late 1980s was driven by a structural change in the drug industry—the development of several multibrand categories in which up to a half-dozen related, but not interchangeable, brands existed, with each commanding a similar price. Formularies gained prominence as a tool for purchasers to use in selecting among these treatment options, with purchasers often obtaining rebates from drug manufacturers in exchange for preferred formulary placement. The cost benefits for patients from choosing a preferred product create incentives for them to ask for specific brands and for plans to attempt to influence doctors to prescribe them.

Congress recognized the importance of formularies in the Medicare Modernization Act of 2003, which created the [Part D retail prescription drug benefit](#) (implemented in 2005). Part D’s reliance on stand-alone private prescription drug plans was based on an assumption that these plans, representing large groups of beneficiaries, would be able to negotiate low prices from pharmaceutical companies in return for preferred placement on formularies. Experts also anticipated that the formulary system would increase the uptake of generic drugs by assigning generic drugs the lowest cost to patients.

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The Centers for Medicare and Medicaid Services (CMS) developed rules in 2006 to control how private plans under Part D create and manage formularies. These included rules on the composition and process for plans' Pharmacy and Therapeutics (P&T) Committees, which recommend formulary placement for individual drugs. These committees generally comprise clinicians (primary care and specialists), pharmacists,

“The original Part D legislation established six protected classes of drugs.”

nurses, legal experts, and administrators. CMS also required annual review of Part D plan formularies to assure adequate coverage: Each formulary must include at least two products in each of fifty-seven designated major therapeutic categories.

CMS also established six protected classes of drugs (anticonvulsants, antidepressants, antineoplastics, antipsychotics, antiretrovirals, and immunosuppressants) for which plans must cover all, or substantially all, medications. This was an effort to ensure that Part D plans would provide patients with broad access to different drugs in these categories. However, it also limited PBM formulary management tools in those classes. To permit more formulary management to lower prices, CMS in 2014 suggested removing protections for three of the six categories. That effort was blocked by Congress, which objected to a number of Part D changes by CMS that year.

The endorsement of the formulary approach as a key element of Part D confirmed trends in other government programs (primarily the Department of Veterans Affairs) and the private sector and established formularies as a well-accepted component of [drug selection and cost control](#).

Formulary Terms

PATIENT COST SHARING

Cost sharing refers to the amount the insured patient pays out of pocket at the point of sale. It can take the form of coinsurance or copays. Coinsurance is usually a percentage of the full cost of a drug; copays are a fixed amount per prescription. Coinsurance is designed to control costs by putting more of the direct cost of expensive products onto the patients who use them. In most cases, formulary drugs are organized into tiers, based on clinical assessments and negotiated prices obtained by the plans. A typical four-tier formulary might include generic, preferred brand, nonpreferred brand, and specialty tiers. Higher-price products appear on the higher tiers and carry the highest coinsurance rates.

Increasing rates of coinsurance and growth in the number of products subject to coinsurance in top formulary tiers have created potential alignment between patient advocates and drug manufacturers around the establishment of limits on the amount of drug costs that fall on patients. Such limits would shift drug expenses from the relatively small percentage of patients taking specialty drugs onto the entire insured population, through increases in other areas such as drug deductibles or full plan deductibles.

A limit on either the percentage size of coinsurance or a patient's total out-of-pocket drug spending would reduce individual patients' financial liability but would confer more upward pricing flexibility for manufacturers and would shift costs to insurers and their subscribers.

UTILIZATION MANAGEMENT

Health and drug plans employ three cost-control tools in conjunction with formularies: prior authorization, step therapy, and quantity limits. These tools restrict the stage at which a drug can be used (for example, after several precursor attempts at treatment with other therapies or non-drug approaches) or limit how much drug can be purchased on one prescription. There is recent [evidence](#) that plans use these tools more frequently in the ACA-established exchanges

than in the employer insurance sector. Part D plans are also slowly incorporating the tools, which have grown to affect 5 percent of the drugs covered by Part D plans, up one percentage point in 2016.

Trends Affecting The Future Of Formularies

RAPID CHANGES TO SPECIALTY DRUG TIERS

The standard lower formulary tiers encourage use of generics and help with selection between therapeutically similar but not interchangeable brands; the top tiers deal with specialty products. The lower tiers are well established with good operating rules and understandable, and generally well accepted, cost-sharing arrangements. The specialty area is in a more difficult and unsettled situation. The high cost-sharing formulas in the specialty tiers are a burden to patients. Some insurers' recent moves to subdivide the specialty tier into separate preferred and non preferred categories suggest that the effort to make the top tier work as a restraint on high specialty prices is still an ongoing project. Exhibit 1 shows such a five-tier formulary structure, in use in 2017 by the BlueCross BlueShield Federal Employee Program.

There is no single common definition of a "specialty" drug. Most definitions are based on five features in which high cost is primary, and there are four other corollaries: The drug must either treat a rare condition, require special handling, use a limited distribution network, or require ongoing clinical assessment. The Medicare Part D drug cost threshold generally sets a floor (\$670 per month in 2017) for defining a drug as specialty.

The top tier is becoming more important as more specialty drugs enter the market and become an increasingly significant part of overall drug expenditures. In particular, a surge in orphan drug approvals has contributed to the expansion of specialty tiers; the Food and Drug Administration approved forty-six new molecular entity orphan drugs over the past thirty months.

America's Health Insurance Plans (AHIP)—the health insurance trade association—forecast in 2016 that over 250 new specialty products would reach the market between 2016 and 2020. Further, AHIP found that almost half of the 150 existing specialty drugs studied "cost in excess of \$100,000 per year, with expenditures for 3 percent of the drugs studied exceeding half-a-million dollars per patient per year." MedPAC has pointed to the impact on Part D spending

EXHIBIT 1

Five-Tier Formulary Design

Tier 1	Generic drugs: Typically the most affordable and are equal to their brand-name counterparts in quality, performance characteristics, and intended use.
Tier 2	Preferred brand-name drugs: Proven to be safe, effective, and favorably priced compared to nonpreferred brands.
Tier 3	Nonpreferred brand-name drugs: These drugs have either a generic or preferred brand available; therefore, patients' cost share will be higher.
Tier 4	Preferred specialty drugs: Proven to be safe, effective, and favorably priced compared to nonpreferred specialty drugs.
Tier 5	Nonpreferred specialty drugs: These drugs typically have a preferred brand available; therefore, patients' cost share will be higher.

SOURCE BlueCross BlueShield Federal Employee Program (adapted).

from the recent entry of new biologics: “Between 2011 and 2014, Part D spending on biologics grew by 31 percent per year, on average. During the same period, specialty-tier drugs, some of which are biologics, grew by 37 percent per year, on average.”

Insurers try to defray their rapidly escalating drug costs by increasing drug deductibles, copays, and coinsurance levels, especially on nonpreferred brand and specialty drug tiers. A [recent analysis](#) of changes in cost sharing by patients taking drugs in the non-preferred brand tiers found a one-year increase of over 13 percent in 2016, across health exchange plans. The higher cost-sharing rates (up to [33 percent on the top specialty tiers](#) of some formularies) create a substantial financial burden for patients receiving treatments with specialty drugs, which often address rare diseases.

COST-SHARING LIMITS

Some states have begun to address high levels of patient cost sharing for drugs through legislative or regulatory action on drug benefits in Medicaid or health exchange plans. This is a fertile area of government interest, supported by both patient advocates and drug manufacturers.

In 2015 [seven states](#) took legislative action to limit patients’ out-of-pocket payments. In 2016 California adjusted rules for Covered California (the state’s health exchange) to cap monthly specialty drug cost sharing at \$250, create a separate pharmacy deductible, and require at least one specialty drug in each category to be included on a lower cost-sharing tier.

A NEW MODEL FOR VALUE ASSESSMENTS

The evolution and acceptance of formularies over the past three decades has been accompanied by a parallel growth and acceptance of P&T committees. This trend may lead to a new model for broader drug value assessment work. There are early efforts to create nongovernmental, independent value assessment groups. The Institute for Clinical and Economic Review, which began full public review operations in 2015, convenes meetings of appraisal committees to review the comparative effectiveness of new products and create baseline assessments of long-term societal benefits and value to short-term drug budgets. Such efforts to create neutral value-assessment groups draw heavily on the experience of P&T committees.

TARGETED THERAPEUTICS AND FORMULARIES

The trend toward very specific, targeted therapeutics for well-defined subsets of patients may change the effectiveness of formularies as a product selection tool in the future. It is a different exercise for plans to try to make substitutions among highly selective tumor-specific oncology products, for example, than to make old-style choices among a group of similar statins or even among tumor necrosis factor inhibitors.

This updated Health Policy Brief corrects errors in the version originally published September 14, 2017.

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Cite as: “Health Policy Brief: **Formularies**,” *Health Affairs*, September 14, 2017. DOI: 10.1377/hpb2017.12

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PHARMACY BENEFIT MANAGERS

On behalf of payers, pharmacy benefit managers negotiate rebates from drug makers in exchange for preferred formulary placement.

Pharmacy benefit managers (PBMs) represent health insurers, self-insured employers, union health plans, and government purchasers in the selection, purchase, and distribution of pharmaceuticals. As brokers between payers (representing patients), drug manufacturers, and dispensers (pharmacies), PBMs play an important and contentious role: They influence which drug products are used most frequently and set terms for how much pharmacies are paid for their part in the process. PBMs are key participants in the administration of drug benefits for more than 266 million Americans with health insurance, using volume-buying leverage to negotiate discounts from manufacturers, generally delivered in the form of rebates. PBMs subsequently share these rebates with their customers—the payers. They also create networks of pharmacies (often supplemented with mail-order operations) and negotiate reduced dispensing fees. PBMs are paid for their services using a mix of fees, retained rebates, and other means. Because they are opaque about the size of discounts obtained, they experience constant scrutiny.

Background

Pharmacy benefit managers became a major force in the late 1980s, expanding from pharmacy claims processing to a business model that forced drug manufacturers to engage in price competition in several drug categories. These categories, including angiotensin-converting enzyme inhibitors, statins, and nonsedating antihistamines, were dominated by multiple similar brand-name drugs that were not suitable for generic substitution. PBMs supported therapeutic interchange by selecting one brand among similar brands in a class as the preferred choice and negotiating discounts from that manufacturer in the form of rebates. That approach lowered the cost of that brand to payers and often lowered direct costs for the patient through placement of the brand on a preferred formulary tier. PBMs were so effective at product selection and earning discounts that three of the early PBMs were purchased by major pharmaceutical companies: Merck (Medco), Eli Lilly (PCS), and GlaxoSmithKline (DPS). That ownership raised concerns among payers that PBMs were favoring certain drugs to the benefit of their parent companies. Such concerns were assuaged when those pharmaceutical companies later sold their PBMs. Merck persevered the longest, owning its PBM Medco until 2003.

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PBMs gained more prominence—and recognition from the federal government—in 2003 with passage of the Medicare Modernization Act (MMA). This law implemented the Medicare Part D outpatient drug benefit using private plans that competed for customers based on their ability to negotiate favorable drug prices, create [formularies](#), and hold down premiums. PBMs generally represent the Part D

“In 2014, the top three PBMs managed pharmacy benefits for over 180 million lives.”

plans in these negotiations. MMA, in fact, includes a noninterference provision, section 1860D-11(i), which restricts direct government involvement in Part D price negotiations.

To be effective as negotiators with pharmaceutical marketers, PBMs need size. The more covered lives (insured customers) represented by a PBM, the more likely that manufacturers will offer rebates in return for potential market share. This reliance on large size has led to consolidation in the PBM industry during the past decade. In 2014 the top three PBMs managed pharmacy benefits for over [180 million lives](#)—about 80 percent of the total number covered by PBMs. Evidencing recent consolidation, two years earlier, when the [Federal Trade Commission](#) approved the acquisition of Medco by Express Scripts, the agency found there were “at least ten significant competitors” in the PBM segment. The current top-three firms represent three different models: the standalone PBM (Express Scripts); the PBM aligned with a major retail drugstore (CVS Health); and a PBM associated with a major health insurer (OptumRx, UnitedHealth Group).

Payers tend to enlist PBMs for their established retail networks, mail-order distribution centers, and experience building and managing continuously evolving drug formularies (Exhibit 1). Perhaps most important, from the payer perspective, PBMs have standing with the pharmaceutical industry in price negotiations.

■ PBMs’ Impact On Drug Expenditures And Prices

PBMs derive revenues from the following sources:

- (1) Fees from their clients (insurers, self-insured employers, union health plans, and government) for administration of claims and drug dispensing;
- (2) A share of the savings from rebates negotiated from drug companies; and
- (3) A combination of fees and shared savings from the maintenance of pharmacy networks.

PBM price negotiations are opaque by design. PBM leaders and their payer clients believe that full transparency on rebate levels could quickly lead to a [floor](#) on bid prices, preventing further discounts.

MEDICARE PART D

The first eight years of drug spending under the Medicare Part D program (from 2006 to 2013) came in well below initial projections: a cumulative \$353 billion spent by Medicare, compared to \$550 billion originally estimated by the Congressional Budget Office (CBO). Some [analyses](#), including a [2014 CBO report](#), attribute lower expenditures primarily to an influx of generic versions of top-selling drugs, lower-than-anticipated Part D enrollment, and a trough period for new drug approvals. PBMs [point to their role](#) in managing prices, utilization, and competition as a complementary force that also served to keep down costs.

It is difficult for the public to know the details of rebate levels obtained by PBMs serving Part D because of the lack of transparency noted above. CBO has found that Part D rebate negotiations reduce drug prices by less than the mandatory Medicaid rebates. Based on 2010 data, CBO describes Medicaid’s “average price of drugs” as “between 27 percent and 38 percent lower than Part D’s average price.” The PBM industry commissioned a 2016 [study](#) that projected \$257 billion in savings to Part D plans from the continued use of PBMs from 2016 to 2025. Using early data from the second year (2007) of Part D experience, the [CBO](#) estimated rebates on single-source brand-name products at 14 percent, a level lower

than estimated rebates in the commercial insurance market.

COMMERCIAL MARKET

It is more difficult to estimate rebate levels in the commercial market. A frequently used industry estimate is that PBMs achieve rebates of 30 percent off list price, accounting for all discounts and fees.

The most meaningful attempts to calculate the size of commercial rebates derive from the difference between invoice prices from manufacturers compared to net receipts to the manufacturer after all discounts and rebates have been deducted. Manufacturers have been more forthcoming with these figures in recent years to explain to the financial community the difference between published prices and subsequent revenues and, on a policy level, to try

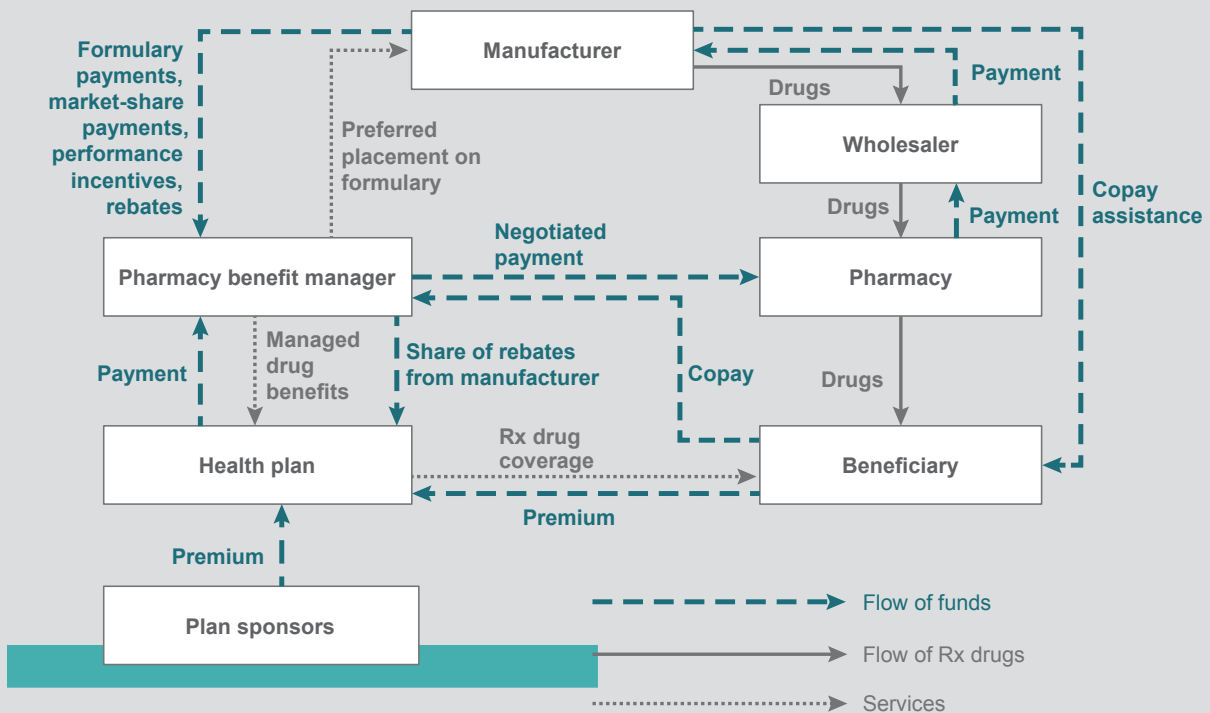
to deflect attention from high introductory list prices and annual price increases.

LAUNCH PRICES

PBMs have less influence with drug manufacturers at the time that initial prices are set, especially when a novel product has no close existing or new competition. However, PBMs can attempt to restrict the impact of new product prices on their clients by limiting early usage. Two recent examples include active efforts to restrain use of hepatitis C and PCSK9-inhibiting cholesterol drugs. PBMs, with Express Scripts as the *most visible advocate*, used public campaigns to highlight the price of the hepatitis C drug Sovaldi and called for tight restrictions to match the limited initial Food and Drug Administration (FDA) labeling of the PCSK9 inhibitors Repatha and Praluent. PBMs inherently stand to benefit from

EXHIBIT 1

The Flow Of Products, Services, And Funds For Nonspecialty Drugs Covered Under Private Insurance And Purchased In A Retail Setting



SOURCE Neeraj Sood, Tiffany Shih, Karen Van Nuys, and Dana Goldman, "Follow the Money: The Flow of Funds in the Pharmaceutical Distribution System," Health Affairs Blog, June 13, 2017.

higher-price products, as high prices create room for high rebates. However, because the primary customers for PBMs are payers, there is a strong countervailing obligation on PBMs to address high launch prices.

Recent Scrutiny Of PBMs

As intermediaries that extract savings for payers from the drug delivery system, PBMs are highly scrutinized by manufacturers and pharmacies. They have also recently drawn attention from public policy makers.

TRANSPARENCY AND SHARING OF REBATES

Recent public interest in deconstructing the components behind high drug launch prices has led to a renewed focus on PBM rebates. The brand-name drug sector has reported its calculation of [the share of invoice prices](#) that go to rebates (26 percent) and the net revenues to the drug manufacturer (63 percent), [taking the position](#) that PBMs and insurers should return more savings directly to patients through clear reductions in cost sharing or reduced premiums.

The Centers for Medicare and Medicaid Services (CMS) has expressed recent interest in more transparency from PBMs and Part D plans on price concessions and pharmacy fees (paid to the PBM, plans, or both) at the point of sale. CMS [cites](#) a recent dramatic increase in post point-of-sale compensation to PBMs, called “direct and indirect remuneration,” with those expenses growing to over 16 percent of Part D gross drug costs in 2015 (or \$22.6 billion in

direct and indirect remuneration out of total Part D gross drug costs of \$137.4 billion). CMS states that one impact of the late point-of-sale adjustments is to increase cost sharing by beneficiaries, with the patient’s cost sharing based on the gross price before these adjustments.

According to PBMs, payers receive an [estimated 90 percent](#) of rebate dollars and factor that income stream into various decisions, including plan premiums and deductibles. However, many small employers get no rebates. Payers don’t necessarily apply drug rebate savings to their drug budgets. To the extent that current public interest in understanding the source of high drug prices turns to the amount and handling of rebates, that discussion is likely to identify PBM activities as a target for policy makers looking for areas to reduce costs.

DRUG LIST PRICES

There is an implied argument from the brand-name drug sector that part of the reason for increases in existing product prices and high launch prices is the growth in rebates paid to the supply chain. A declining share of invoice prices being captured by manufacturers (from 67 percent in 2013 to 63 percent in 2015) puts pressure on manufacturers to increase the list sales price to maintain profit levels. The PBM industry refutes that contention with a [study](#) claiming that there is no correlation between price increase levels and average rebates.

This updated Health Policy Brief corrects errors in the version originally published September 14, 2017.

HealthAffairs

Health Policy Briefs are produced under a partnership of *Health Affairs* with the generous support of the Commonwealth Fund and Memorial Sloan Kettering Cancer Center. Text highlighted in blue is hyperlinked to outside sources in the online version of this brief.

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Cite as: “Health Policy Brief: Pharmacy Benefit Managers,” *Health Affairs*, September 14, 2017. DOI: 10.1377/hpb2017.13

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PRESCRIPTION DRUG PRICING

POLICY OPTIONS PAPER

MARCH 15, 2018

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Improving The Affordability Of Specialty Drugs By Addressing Patients' Out-Of-Pocket Spending

ABSTRACT Spending on outpatient prescription drugs has increased dramatically in recent years. At the same time, the affordability of specialty drugs has eroded, in part because of cost-sharing provisions on commercial insurance and Medicare Part D plans. In this brief we focus on patients facing high out-of-pocket spending for prescription drugs as a result of the growing use of deductibles and coinsurance. We discuss how current cost-sharing provisions and high drug prices threaten the affordability of drugs, and we provide policy recommendations to ensure greater out-of-pocket cost protection for patients. Solutions that limit Medicare beneficiaries' total spending on drugs or enhance pre-deductible coverage for chronically used medications under Medicare and commercial plans may be politically feasible. Policies that include consideration of value for establishing cost sharing and coverage are more challenging to implement but may be a more promising long-term strategy.

Spending on outpatient prescription drugs has increased markedly in recent years. National health spending for retail prescription drugs (excluding physician-administered drugs) totaled \$328.6 billion in 2016 following two years of notable spending growth.¹ Much of this spending growth is attributed to the rise in the use of so-called specialty drugs.^{2,3} The Centers for Medicare and Medicaid Services (CMS) defines a product as "specialty-tier eligible" when the sponsor-negotiated price is \$670 per month or more.⁴ However, most specialty drug spending is concentrated on products used for rare, complex, and life-threatening conditions. These products include medications for HIV (average monthly price per fill: \$1,556), inflammatory conditions (\$3,588), multiple sclerosis (\$5,056), oncology (\$7,891), and hepatitis C (\$15,708).² Among drugs offered through outpatient pharmacy benefits, specialty drugs currently make up only 1–2 percent of use but 40–50 percent of drug spending,^{2,5} making them an important target for payers and policy makers alike.

Recent drug price increases and insurance coverage changes threaten patients' access to specialty drugs by reducing their affordability. High prices may create incentives for plans to reduce the generosity of coverage for some products, as has been noted for high-price drugs offered under the Medicare Part D benefit^{6–10} and through the growing use of deductibles and coinsurance among commercial payers.^{11,12}

One of the principal concerns related to the rise in direct patient cost sharing for specialty drugs is severe personal or family financial burden because of illness,

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a problem that has been termed “financial toxicity.” Commonly reported “symptoms” of financial toxicity include exhausting savings accounts, having to remortgage a home, needing to borrow money from family or friends, or seeking bankruptcy protection.¹³ Financial toxicity is associated with nonadherence to medications,^{14–22} and there is emerging evidence that it adversely affects quality of life and survival.²³ It is also well documented that higher cost sharing or unexpected changes in costs for prescription drugs can reduce patients’ uptake of and adherence to treatments, including specialty drugs.^{10,14,15,24–32}

In this brief we document how some of the cost-sharing provisions in commercial insurance and Medicare Part D plans have led to higher out-of-pocket spending and unprecedented levels of financial toxicity for patients needing specialty medications. Because coverage policies regarding pharmacy benefits can differ from those for medical benefits, we focus on prescription drugs offered under out-

“Much of this spending growth is attributed to the rise in use of specialty drugs.”

patient pharmacy benefits and Medicare Part D, excluding physician-administered drugs. We provide several policy solutions to improve the affordability of specialty drugs by targeting patients’ out-of-pocket spending. We also suggest methods that payers may consider to align the generosity of coverage with a drug’s value in terms of both clinical benefit and cost.

■ Drug Coverage In The US

In 2016 private health insurance and Medicare accounted for 43 percent and 29 percent of retail drug spending, respectively.¹ Cost sharing—the requirement that patients contribute financially to services obtained when using their health insurance—has historically served the purpose of reducing “moral hazard,” or the overuse of services that are provided at a low marginal cost.³³ However, the level of cost

sharing required for specialty medications has risen in recent years and may undermine the appropriate use of specialty drugs. Ideally, cost sharing should be designed to steer patients toward the most cost-effective treatments when more than one treatment exists. In the case of relatively expensive specialty medications, for which therapeutic alternatives are limited or nonexistent, cost-sharing requirements may serve mainly to impede access to treatment altogether rather than to deter “overuse.”

Contributing to the increase in cost sharing, both commercial and Medicare Part D plans have shifted away from copayments (where the patient pays a flat dollar amount per prescription) and toward greater reliance on deductibles (where the patient pays 100 percent of the drug’s negotiated price until the deductible is met) and coinsurance (where the patient pays a predetermined percentage of the drug price).

COMMERCIAL INSURANCE

In 2016, 196 million Americans had commercial health insurance,¹ and most plans covered prescription drugs.³⁴ Coverage of prescription drugs in commercial insurance plans varies widely, but most require some form of patient cost sharing, with different tiers for generics, brands, and specialty drugs. Commercial plans also typically have a maximum out-of-pocket limit for cost sharing, which applies to prescription drug coverage. For example, for commercial plans sold through exchanges created under the Affordable Care Act (ACA), the limit was \$7,150 for an individual and \$14,300 for a family in 2017.³⁵

For people in exchange (Marketplace) plans, exposure to out-of-pocket prescription expenses can vary, despite standardization of policies by metal tiers, annual maximums on out-of-pocket spending, and the availability of cost-sharing subsidies for beneficiaries with incomes between 100 and 250 percent of the federal poverty level.³⁵ Most bronze plans (lower-premium plans with the lowest actuarial value) have combined medical and prescription drug deductibles that do not begin to cover an enrollee’s costs until the deductible has been met. In bronze plans, the average combined deductible was more than \$5,700 in 2016.³⁶ However, most silver, gold, and platinum plans have separate medical and drug deductibles (or no deductible for drugs); for these plans, the average

deductibles ranged from \$12 in platinum plans to \$404 in bronze plans in 2016.³⁶

Patients in employer-sponsored plans are now paying more of their out-of-pocket expenses for retail prescriptions in the form of deductibles and coinsurance, as opposed to copays. For example, deductibles grew from 4 percent of cost-sharing payments in 2004 to 24 percent in 2014; coinsurance increased from 3 percent to 20 percent over that same period.³⁷ In 2014 an estimated 10-15 percent of people with drug coverage through employer-sponsored coverage who are treated for one of several high-cost conditions (cancer, mental illness, digestive disease, or endocrine, circulatory or blood disorders) spent over \$5,000 annually out of pocket on retail and nonretail drugs.³⁸

MEDICARE

Since 2006 Medicare has offered voluntary prescription drug coverage to seniors and younger adults with permanent disabilities through the Part D program. In 2017, over 70 percent of Medicare beneficiaries received prescription drug coverage under Part D (through either a private, stand-alone Part D plan or a Medicare Advantage plan that includes the Part D benefit), rather than through an employer-sponsored retiree benefit or other coverage source.³⁸

In general, plans must include on their formularies at least two drugs in every drug class, but plans vary in terms of their specific benefit design, cost-sharing amounts, utilization management tools, and covered drugs. In 2017 a majority of Part D enrollees are in plans with a separate tier for specialty drugs, with coinsurance ranging from 25 percent to 33 percent in the initial coverage phase.³⁹ Beneficiaries with low incomes and modest assets are eligible for assistance with Part D plan premiums and cost sharing, but most Part D enrollees (68 percent in 2015) do not receive this assistance.³⁸

In 2017 the standard Part D benefit included four phases: a \$400 deductible; an initial coverage phase with coinsurance of 25 percent until drug spending reaches \$3,700; a “coverage gap” with coinsurance of 40 percent until total out-of-pocket spending reaches \$4,950; and catastrophic coverage, in which the beneficiary is responsible for paying up to 5 percent of their medication costs for the remainder of the year.

Beneficiaries who do not receive low-income subsidies can face substantial out-of-pocket spending for prescriptions, particularly if they use expensive specialty drugs or multiple higher-cost brand-name drugs.^{7,40,41} Unlike most commercial drug benefit plans, Part D does not include a hard, annual cap on

“A majority of Part D enrollees are in plans with a separate tier for specialty drugs.”

out-of-pocket expenses. When beneficiaries take medications costing tens of thousands of dollars per year or more, their out-of-pocket spending in the catastrophic phase can exceed their spending in the other benefit phases combined.⁴⁰ Because progression through the Part D benefit relies almost exclusively on percentage-based cost sharing for specialty drugs, rising drug prices result in more beneficiaries facing the coverage gap and catastrophic phases of the benefit over time.⁴¹⁻⁴³

Furthermore, most plans use drugs' point-of-sale prices—instead of net prices that are achieved as a result of plan negotiated rebates—as the basis for calculating patient cost sharing and progression through the Part D benefit.⁴³ This is a key contributor to the higher proportion of beneficiaries entering the catastrophic coverage phase of the benefit over time, from 17 percent of non-low-income subsidy enrollees in 2007 to 26 percent in 2014.^{44,45}

Proposed Policy Solutions

Given current and potentially increasing affordability challenges for Medicare beneficiaries and commercial plan enrollees who need specialty drugs, we suggest several options to reduce financial toxicity among patients and potential challenges to consider.

USE COPAYMENTS INSTEAD OF COINSURANCE

The use of copayments for preferred drugs—instead of coinsurance and deductibles—may improve patients' access and adherence to treatments by providing more predictability for out-of-pocket expenses for those with chronic medication needs.

There are two primary challenges related to the proposal to use copayments instead of coinsurance. First, patients may be less price-sensitive when paying a copayment than when their out-of-pocket payment is proportional to a drug's price. However, plans may still differentiate between preferred and nonpreferred products through use of copayment tiers (with lower copayments for preferred products) to steer patients to more cost-effective treatments when competitors exist within a specialty drug class. Second, implementing this proposal within Medicare Part D would require a statutory change to the standard benefit design, which currently requires coinsurance during the coverage gap, regardless of a plan's cost-sharing design in the initial coverage phase.

SHARE REBATES WITH PATIENTS

Another option for managing patient cost sharing under Medicare or private drug plans is to base it on the plan's net prices (post-rebate) for drugs rather than on drug prices at the point of sale (before rebates and price concessions are received).⁴⁶ For branded specialty drugs with competitors, rebates obtained by health plans and pharmacy benefit managers may be substantial, yet patients paying deductibles and coinsurance for these drugs do not benefit from such price reductions directly. There is a stunning lack of transparency about the magnitude of rebates under current arrangements, which places consumers of specialty drugs at a disadvantage. Plans argue that rebates are used to hold down premium costs for all insured people, but this may happen at the direct expense of patients needing high-price specialty drugs.

To reduce out-of-pocket spending for patients paying coinsurance or deductibles, plans could pass through estimated rebates to the patient directly at the point of sale. Importantly, pass-through of rebates would

large—this could result in substantial cost savings for patients using these drugs.

There are several challenges to this method of reducing patient cost sharing. First, plans would need to estimate the size of the rebate at the point of sale for an individual product, which would likely increase administrative burden. Second, rebates might not be large for some drugs, including specialty drugs that have limited competitors, meaning that cost savings for patients who take those drugs would be minimal. Third, although empirical evidence is limited, it is possible that disclosing rebates for individual products or payers could disadvantage payers' negotiations, potentially resulting in higher prices (lower rebates). To mitigate this concern, payers could be required to provide access to discounted (post-rebate) prices that have been aggregated in some form across types of drugs to prevent disclosure of product-specific rebates. Finally, to the extent that plans currently use rebates to offset total premium costs, passing through rebates at the point of sale instead may result in an increase in premiums across all members.

ALIGN COST SHARING TO REFLECT VALUE

Recently, there has been increased focus on value-based formularies for prescription drugs (also known as value-based insurance design).⁴⁷ For drugs that provide high value for preventing disease or managing disease progression, payers could use benefit design to reduce the chances of nonadherence or treatment interruption. Drugs used to prevent chronic disease progression or complications could be exempt from deductibles or subject to preferred (or zero) cost sharing. Doing so would ensure that patients needing ongoing medication therapy could continue to receive treatment without cost-related disruptions that could occur when benefits reset in each new plan year.⁴⁷

Evidence from value-based health plan design has focused primarily on chronic disease medications with generic competitors, but this approach could also be used to offer specialty drugs with very high clinical benefit to patients with less out-of-pocket obligation. Conceptually, it would be reasonable to steer patients to the most effective option within a specialty class (for example, the best tumor necrosis factor inhibitor for rheumatoid arthritis). Practically, physicians and

“Recently, there has been increased focus on value-based formularies for prescription drugs.”

provide savings to Medicare Part D enrollees in each benefit phase without requiring modifications of the standard benefit design. For drugs with multiple treatment options—where rebates are thought to be

possibly patients will voice concerns about such an approach because of the clinical differences among products. Placing such coverage policies within the context of pragmatic trials or within Medicare demonstration projects may be one approach to allay concerns about preferential treatment within specialty drug classes.

LIMIT OUT-OF-POCKET SPENDING IN PART D

Medicare Part D does not currently have an annual out-of-pocket spending maximum for outpatient prescription drugs; this is true in both stand-alone drug plans and Medicare Advantage plans. Policy makers could place a limit on out-of-pocket prescription drug spending in Part D by removing the 5 percent coinsurance payment from the catastrophic phase of the benefit and limiting enrollees' annual cost sharing to the total out-of-pocket spending amount that currently triggers catastrophic coverage (\$4,950 in 2017). In 2015, 3.6 million Medicare Part D enrollees had drug spending above the catastrophic threshold, with one million of these enrollees having no low-income subsidy to minimize out-of-pocket spending.⁴¹

A key challenge to this proposal is that pharmaceutical companies might respond by simply raising drug prices, because patients would not be price-sensitive after reaching the catastrophic coverage phase. Such tendencies could be mitigated, however, if Part D plans had a stronger financial incentive to negotiate larger rebates for higher-price drugs and to take more steps to manage the use of these drugs by their enrollees. Providing plans with such incentives could produce savings for enrollees, Medicare, and the plans themselves. For example, plans could be given greater financial responsibility for Part D spending in the catastrophic coverage phase (currently, plans are required to pay only 15 percent in this phase, compared to 75 percent in the initial coverage phase). A similar proposal has been suggested by the Medicare Payment Advisory Commission.⁴⁵

Capping Part D spending would likely raise premiums across all beneficiaries, as current beneficiary spending in the catastrophic phase would need to be incorporated into program costs and redistributed across all insured people. In 2014, 3.6 million Part D beneficiaries reached catastrophic spending (out of 41 million beneficiaries in the Part D program),

a dramatic increase from prior years.⁴⁴ Up-to-date estimates of beneficiaries' spending in catastrophic coverage and the possible impact on premiums are needed to determine whether such increases will be palatable to beneficiaries and policy makers.

Conclusion

We have provided an overview of key affordability challenges for patients needing high-cost specialty outpatient prescription medications. We have excluded specific discussion of drugs offered under Medicare Part B and commercial inpatient or outpatient medical coverage. However, some concerns noted regarding the increasing use of high deductibles and coinsurance would also apply to physician-administered medications.

We have discussed several proposals for limiting out-of-pocket spending for patients covered under commercial insurance and Medicare Part D. Data do not currently exist to determine empirically which of these options would provide the greatest net benefit to patients and payers. However, there may be political support for several proposed options, including removing catastrophic coinsurance on Medicare Part D and passing through estimated rebates at the point of sale.

In November 2017 the National Academies of Sciences, Engineering, and Medicine advanced similar recommendations targeting the affordability of medicines,⁴⁸ and CMS released a request for information for policy approaches for applying rebates and price concessions to drug prices at the point of sale in Medicare.⁴⁹ These are promising steps toward identifying the feasibility and impact of such a policy change.

Policies that provide patients with pre-deductible access to chronically used drugs or those that prevent increased medical spending may help avoid disruptions in ongoing disease management. This type of benefit design could be applied to both Medicare and commercial plans. More complex policies that include consideration of value in establishing cost sharing and coverage are more challenging to implement but may constitute a more promising long-term strategy. Evidence of their impact is sorely needed.

It will be important to monitor the extent to which our proposed solutions result in higher prices for payers, enrollees/beneficiaries, and society. Stakeholders should explore these options to determine the impact of their implementation on per member per month premium increases and whether they have spillover effects on other components of health spending as a result of potentially improved uptake of and adherence to prescribed drugs.

Our proposed solutions primarily focus on reducing patients' out-of-pocket spending through benefit design changes. These solutions do not address

prescription drug affordability challenges for patients who lack health insurance coverage entirely or non-cost related drug access restrictions faced by Medicaid patients. These solutions also do not target the underlying prices of drugs, which are directly connected to affordability for patients who are required to pay a percentage of a drug's list price. Underlying drug prices also affect total insurer spending (which affects premiums for all insured people). However, these proposed options offer possible steps toward ensuring greater affordability for some insured patients who need costly medications.

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Health Affairs

Policy Options Papers are produced under a partnership of *Health Affairs* with the generous support of the Commonwealth Fund and Memorial Sloan Kettering Cancer Center.

Cite as: “Policy Options Paper: Improving The Affordability Of Specialty Drugs By Addressing Patients’ Out-Of-Pocket Spending,” *Health Affairs*, March 15, 2018. DOI: 10.1377/hpb20180116.800715

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PRESCRIPTION DRUG PRICING

POLICY OPTIONS PAPER

MARCH 15, 2018

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Promoting Competition To Address Pharmaceutical Prices

ABSTRACT Under ideal market conditions, competition among producers of a commercial good can drive down prices. The market for pharmaceuticals, however, is inefficient in many ways, leading to rapid price increases in recent years, even for some drugs without patent protection. This brief surveys the two principal types of pharmaceutical competition—inter-brand and brand/generic—and examines the reasons they may fail to produce lower prices for patients, including the absence of information on comparative efficacy, lack of federal agency authority to consider drugs' value, narrow drug substitution laws, and laws that prohibit formulary exclusion. The brief then reviews the policy interventions that could help address these shortcomings. Such proposals include increasing the efficiency of generic drug approval, allowing temporary importation of drugs during domestic shortages or price fluctuations, and discouraging the improper use of patent exclusivities.

It is a common understanding that competition generally lowers prices. However, the price-lowering impact of effective competition depends on certain market characteristics, such as substitutable products, many sellers, independent buyers, meaningful information, and low barriers to entry.¹⁻⁴ In US pharmaceutical markets, many of these assumptions do not hold, especially for new drugs.

An Imperfect Market

New drugs, and some older ones, are generally sold by a single manufacturer. Entry of competitors may be limited by high start-up costs, approval requirements, and patents or other exclusivities (such as those contingent on a drug receiving regulatory approval) that legally restrict competition by preventing other manufacturers from selling the same drug or formulation.⁵ Products in the same therapeutic class may be studied in different populations or at different doses, which frustrates attempts to compare them to each other. Pricing is obscured by a labyrinthine system of rebates, spreads, discounts, coupons, and nontransparent business arrangements, particularly between pharmacy benefit managers and manufacturers.⁶ Patients are not independent purchasers since they require authorization from prescribers, while insurance companies can alter patients' observed prices.

In this highly imperfect market environment, manufacturers can maintain high prices or raise low prices suddenly without attracting meaningful competition. Certain drugs for multiple sclerosis, rare diseases, and cancer cost more than \$60,000,⁷ \$300,000,⁸ or \$450,000^{9,10} per patient per year, respectively. Even

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old drugs are not exempt. In 2015 former hedge fund manager Martin Shkreli made headlines as CEO of a small pharmaceutical enterprise by raising the price of pyrimethamine (Daraprim), an anti-protozoal first approved in 1953,¹¹ by 4,000 percent to \$750 per

“US drug makers can maintain high prices or raise low prices suddenly without attracting meaningful competition.”

pill.¹² Although pyrimethamine’s price increase was unusual in its magnitude, it was emblematic of a broader phenomenon: In a recent one-year period, the prices of over 1,200 generic drugs—nearly 10 percent of all generic drugs—increased by an average of 448%.¹³

Pharmaceutical competition can be divided into two broad types: inter-brand and brand/generic.¹⁴ This brief outlines the current marketplace in the US for each type and evaluates policy levers that could increase competition and lower prices.

Inter-Brand Competition

Inter-brand competition can occur among chemically distinct drugs that treat the same disease. This type of competition is not diminished by patents or other exclusivities, since these exclusivities generally extend to a specific chemical substance, not to a distinct substance that treats the same disease.

Some competing drugs with different chemical structures have the same or similar mechanisms of action. For example, lovastatin (Mevacor) was approved in 1987 as a cholesterol-lowering agent that reduces cardiovascular risk. In subsequent years, pravastatin (Pravachol), simvastatin (Zocor), rosuvastatin (Crestor), and others were approved for similar uses based on similar mechanisms of action. However, there can be differences in safety or effectiveness, even among drugs with the same mechanism of action. For example, atorvastatin and rosuvastatin emerged as having higher enzyme inhibition potency, making them more useful for some high-risk patients.¹⁵

Inter-brand competition can also occur among drugs in different therapeutic classes. The market for gastroesophageal reflux disease is composed of ant-acids, H₂ receptor blockers, proton-pump inhibitors, and other classes. In some cases, drugs also compete with nondrug treatments. Proton-pump inhibitors, for example, have dramatically reduced the need for gastric surgery.¹⁶

Inter-brand competition among drugs can sometimes lead to lower prices.^{17–24} The 2013 launch price of sofosbuvir (Sovaldi), a direct-acting antiviral for hepatitis C, was \$84,000, while competitor glecaprevir/pibrentasvir (Mavyret) was launched in 2017 at \$26,400 amidst growing competition.^{25,26}

In many cases, however, inter-brand competition does not lower prices. The tyrosine kinase inhibitor imatinib (Gleevec) was introduced to treat chronic myelogenous leukemia in 2001 at a price of \$26,400 per year. Over the next decade, multiple other tyrosine kinase inhibitors were approved for the same indication, but imatinib’s list price continued to rise to over \$120,000 per year.²⁷

Several factors that mitigate the potential price-lowering effects of inter-brand competition include the perception of price as a signal of efficacy, imperfect information, and legal mandates on purchasers.

PRICE AS A SIGNAL

Consumers often view high price as a signal of superiority, whether or not such an impression is justified by therapeutic benefit.^{28,29} Rosuvastatin entered the market in 2003, with pricing for its 10 mg dose slightly higher than best-selling atorvastatin,³⁰ and maintained its price even after generic atorvastatin was introduced in 2011. Similarly, AstraZeneca launched esomeprazole (Nexium) at a similar price to its nearly identical older drug omeprazole (Prilosec), even though the evidence demonstrated comparable efficacy,³¹ and continued to generate substantial sales from esomeprazole years after generic and over-the-counter versions of omeprazole were introduced.

IMPERFECT INFORMATION

In many cases, the absence of comparative effectiveness information can frustrate price competition. Many new drugs obtain Food and Drug Administration

(FDA) approval based on single-arm or placebo-controlled trials, producing no direct comparative data to facilitate evidence-based prescribing or use.³²

LEGAL MANDATES ON PURCHASERS

Inter-brand competition is also weakened if payers cannot leverage the threat of formulary exclusion during price negotiations. US laws limit formulary exclusion in major sections of the market. For example, Medicare Part D programs cannot exclude cancer drugs or any of five other protected drug classes.^{33,34} Many states have laws that prevent private payers from excluding cancer drugs from their formularies.³⁵ Within Medicaid, individual states can negotiate discounts but are required to cover nearly all FDA-approved drugs regardless of price or value. Without the ability to exclude drugs from formularies, payers lose their most potent means to negotiate rebates or discounts, and inter-brand competition can evaporate.^{36,37}

Formulary exclusion is not the only means to limit the use of high-cost, low-value drugs. For example, some payers can impose patient copayments or other cost sharing to discourage use. However, manufacturers have partially neutralized these efforts by offering copay “coupons” to help defray patient out-of-pocket expenses or by supporting nonprofit patient assistance programs that fulfill a similar role.^{38,39}

Brand/Generic Competition

In contrast to the complex dynamics of inter-brand competition, the introduction of generic substitutes for brand-name drugs tends to exert unambiguous, downward price pressure.⁴⁰ This effect is driven by state drug product selection laws, which permit or mandate pharmacists to substitute FDA-approved generic drugs unless physicians explicitly refuse substitution. Both the speed and extent of price decreases resulting from generic entry have intensified, with prices for oral generic medicines now declining, on average, to approximately 50 percent of the cost of the branded product within about six months of generic entry, and to approximately 10 percent within 2.5 years.⁴¹ Prices also decline as more generics enter the market, on average falling to approximately 77 percent of the brand price with two generic com-

petitors and to approximately 60 percent with three generic competitors.^{42,43}

EXCLUSIVITIES

Patent terms end twenty years from the patent application filing date, but applications are often filed years before FDA approval. To compensate for some of this lost exclusivity, the term of one patent may be extended up to five years, and the extension cannot result in a patent expiration date that is more than fourteen years after FDA approval.⁴⁴

“Secondary” patents covering modifications to the drug (such as new formulations, manufacturing processes, or peripheral features) are often obtained shortly before original patents expire, potentially providing extended exclusivity. But secondary patents tend to be narrower and weaker than substance patents, and generic manufacturers successfully invalidate many of them in court, though litigation itself can delay generic entry and increase market entry costs.

Congress has also created nonpatent exclusivities to incentivize the development of new drugs or new information about existing drugs. These exclusivities limit the FDA’s ability to approve generic competitors. For example, to incentivize the development of drugs for rare diseases, the 1983 Orphan Drug Act created an exclusivity period of seven years from the date of FDA approval.⁴⁵ The Hatch-Waxman Act of 1984 provided exclusivity periods of about five to seven years from the date of FDA approval for all new chemical entities and three years for new approvals that require the submission of new clinical investigations, such as to support a new indication for an existing drug.⁴⁶ In 1997 the FDA Modernization Act established a six-month extension to the end of patent or other exclusivity periods to incentivize studies on pediatric populations,⁴⁷ and in 2009 Congress provided twelve years of exclusivity for new biologics.⁴⁸

STALEMATE OVER EXCLUSIVITY DURATION

The creation of these nonpatent exclusivities has coincided with an increase in the number of patents per drug,⁴⁹ creating concerns of excessively long monopolies. At the same time, generic drug manufacturers have intensified their efforts to bring patent challenges. More than 90 percent of brand-name

drugs with annual sales exceeding \$250 million now experience patent challenges, which begin an average of 5.2 years after FDA approval.⁵⁰ On average, more than four patent challenges are now addressed to each drug.⁵⁰ As brand-name and generic manufactur-

“The absence of comparative effectiveness information can frustrate price competition.”

ers have battled over the duration of market exclusivity, the average period between FDA approval and first generic entry has remained relatively constant, at approximately 13.5 years, since at least the mid-1990s.⁵⁰⁻⁵³

■ Competition Policy Options

While inter-brand competition has not consistently lowered drug prices, strong generic competition has done so reliably. Policy makers interested in reducing drug prices through competition therefore must both facilitate more effective inter-brand competition and ensure the timely availability of generic drugs.

EFFECTIVE INTER-BRAND COMPETITION

The following policy strategies would help to facilitate more effective competition among brand-name drugs: enhancing government authority for value assessments; broadening of substitution laws; and using evidence-based formularies.

Enhance Authority For Value Assessment: Better information about drug value would strengthen inter-brand competition by helping patients and physicians decide which drug is the most effective and cost-effective.⁵⁴ Policy makers could enhance the authority of federal agencies or designated nonprofits to evaluate and disseminate information about drug value,⁵⁵ as is done in other countries.⁵⁶ Filling this role in the United Kingdom and Germany, for example, are the National Institute for Health and Care Excellence and the Institute of Quality and Efficiency in Healthcare, respectively.

In the US, however, the FDA lacks the authority to reg-

ulate prices or to condition approval on value or cost, and no government agency focuses on evaluating or clearly communicating the value of treatments after approval. The Patient-Centered Outcomes Research Institute (PCORI) was established in 2010 to broadly evaluate prevention efforts, diagnostics, treatments, and services, but comparative drug evaluation constitutes only a small fraction of PCORI's remit, and it is not authorized to consider cost.⁵⁷ Past federal attempts to initiate value assessments have been thwarted by political pressure. The Office of Technology Assessment was created in 1972 but disbanded in 1995.^{58,59} Currently, the Agency for Healthcare Research and Quality (AHRQ) conducts and supports health services research to enhance decision making and improve health care delivery, but it has supported few pharmaceutical cost-effectiveness studies. AHRQ's potential to fill this role may be reduced further, as the FY2018 budget diminishes its funding and institutional independence.⁶⁰

During the process of passing the Affordable Care Act in 2010, it was expected that PCORI would help guide clinical decision making, but political forces also altered that group's role. Its potential for supporting evaluations of high-price treatments was reduced not only by the absence of authority to consider cost but also by an explicit prohibition against the use of quality-adjusted-life-year thresholds.⁶¹

Some nonprofit organizations have sought to fill this void of comparative evidence, including the Institute for Clinical and Economic Review, the Alosa Foundation, and Consumer Reports Best Buy Drugs,⁶² but these organizations have only a fraction of a federal agency's resources.

Broaden Substitution Laws: Another option to promote inter-brand competition is to broaden state substitution laws to allow pharmacies to dispense different chemical entities in the same therapeutic category (“therapeutic substitution”). Many pharmacy benefit managers have programs encouraging prescribers to engage in therapeutic substitution to minimize the use of high-price, low-value drugs. Similarly, Medicaid programs can narrow drug indications or impose prior authorization or step-therapy requirements to ensure that cheaper but equally effective alternatives are tried first. Currently, however, therapeutic substitution requires explicit physician autho-

rization. Policy makers could extend greater latitude for discretionary or automatic pharmacy substitution of similar dosage forms (for example, tablet versus capsule) or different drug-device combinations, after evaluation to ensure that the patient experience will be comparable.

Encourage Evidence-Based Formularies: Another approach is to permit government payers more flexibility in constructing evidence-based formularies that exclude low-value drugs. In 2017 Massachusetts proposed to create a closed formulary for its Medicaid program. Employed by most commercial payers, closed formularies allow payers to select which drugs are covered based on criteria such as clinical effectiveness and cost. One persistent concern about such arrangements, however, is that useful drugs might be excluded inappropriately. To minimize this problem, Massachusetts proposes to maintain an exceptions process for patients with demonstrated need. The Department of Veterans Affairs has successfully operated a closed formulary, contributing to its obtaining some of the best drug prices among public payers.⁶³

MORE EFFICIENT GENERIC ENTRY

While generic competition generates lower-cost substitutes, the intensity of such competition is primarily dependent on the number of manufacturers.⁶⁴ As long as a generic drug market with multiple

independent participants is maintained, prices can stabilize at levels far below the price of the original branded product.⁴³ Some markets, however, have few competitors.

Over the past few years, the generics market has experienced sudden shifts in prices (exhibit 1). For example, the price of albuterol sulfate tablets, used for asthma, jumped 3,000 percent from 2012 to 2014, amidst allegations of price fixing.^{65,66} The price of digoxin, used to treat heart failure, rose 635 percent as five of the eight manufacturers operating in 2002 exited the market.⁶⁷ In some cases, competition was disrupted by active pharmaceutical ingredient shortages, causing input prices to swell and in turn prompting some manufacturers to leave the market. When shortages resolve, former manufacturers might not re-enter.

Single-source products are particularly vulnerable to price increases. The price of albendazole (Albenza), an old anti-parasitic drug, rose from \$6 to \$120 per dose between 2010 and 2013, after rights to the drug were purchased from the existing sole supplier. The new company's revenue-generating strategy was aided when the manufacturer of a related product left the market shortly thereafter.

Absent transaction costs, these types of price spikes among non-patent-protected drugs should be mitigated by the market entry of additional sellers.

EXHIBIT 1

Examples of unpatented drug price increases and key causative factors

Drug name (brand name)	Use	Price increase	Key factors in price increase
Pyrimethamine (Daraprim)	Toxoplasmosis	From \$14 to \$750/tablet ^a	Single manufacturer
Corticotropin (H.P. Acthar Gel)	Seizures	From \$40 to \$23,000/vial ^b	Single manufacturer
Digoxin (Lanoxin)	Heart failure	From \$0.11 to \$1.10/tablet ^c	Manufacturers leave market
Albendazole (Albenza)	Parasitic infection	From \$6 to \$119/dose ^b	Single manufacturer, exit of close competitor
Colchicine (Colcrys)	Gout	From \$0.09 to \$4.85/pill ^d	3-year exclusivity
Hydroxyprogesterone caproate (Makena)	Preterm labor	From \$15 to \$1,440/dose ^e	7-year orphan exclusivity
Doxycycline (multiple)	Bacterial infection	From \$20 to \$1,849/bottle ^f	Shortage, alleged collusion

SOURCE Authors' analysis of information from the following sources. ^aSternberg S. Skyrocketing prices for generic drugs compromise health care. U.S. News [serial on the Internet]. 2015 Dec 8 [cited 2017 Dec 15]. Available from: <https://www.usnews.com/news/articles/2015/12/08/skyrocketing-prices-for-generic-drugs-compromise-health-care?int=news-rec>. ^bKesselheim AS. Why are some generic drugs skyrocketing in price? Hearing before the Subcommittee on Primary Health and Aging, US Senate. 2014 Nov 20. ^cCummings EE. Why are some generic drugs skyrocketing in price? Hearing before the Subcommittee on Primary Health and Aging, US Senate. 2014 Nov 20. ^dKesselheim AS, Solomon DH. Incentives for drug development: the curious case of colchicine. *N Engl J Med*. 2010;362(22):2045-47. ^ePatel Y, Rumore MM. Hydroxyprogesterone caproate injection (Makena) one year later. *Pharmacy & Therapeutics*. 2012;37(7):405-11. ^fMohney G. Generic drug price sticker shock prompts probe by Congress. ABC News. 2014 Nov 21.

However, entry into the generic drug market requires time for product formulation, quality assurance, bioequivalence testing, and FDA review.⁶⁸ Even when prices have risen dramatically, generic firms may be hesitant to make such investments, knowing that the incumbent could quickly lower its price, minimizing the expected profits of the potential entrant.

The following strategies could help reduce market-entry barriers and ensure the availability of more ge-

“Introduction of generic substitutes for brand-name drugs exerts unambiguous downward price pressure”

neric competitors: reductions in FDA approval times; importation from foreign countries; and the curbing of abuses of exclusivity.

Reduce Approval Times: The Generic Drug User Fee Act (GDUFA) of 2012 aimed to accelerate new generic entry by imposing “user fees” that would allow the FDA to hire staff to reduce the average application review period from thirty-one months to ten months.⁶⁹ In 2017 the FDA Reauthorization Act (FDARA) continued these fees for another five years at higher levels. FDARA also authorizes the FDA Office of Generic Drugs to accelerate applications to address drug shortages or insufficient competition, such as in cases where there are three or fewer competitors.^{70,71} In 2017 the FDA announced a Drug Competition Action Plan that includes efforts to limit “gaming” of the system, reduce regulatory obstacles to generic drug approval, and improve FDA communication with generic applicants; however, the implementation and impact of this plan remain to be seen.⁷²

Allow Importation: During times of shortage, policy makers could allow temporary importation of generic drugs from countries with similar regulatory environments, until competitors can enter the market and stabilize domestic supply.⁷³ Drugs with few US manufacturers and low domestic demand, but high demand outside the US, could be identified using the FDA’s

database of approved drug applications and commercial databases showing consumption by country.

Curb Exclusivity Abuses: Policy makers can also take steps to enhance generic competition by ensuring that brand-name manufacturers do not block generic entry by obtaining multiple overlapping patents or leveraging available exclusivities improperly. For example, patents are lawfully available only for inventions that are novel and nonobvious. Yet lax enforcement of patenting standards means that manufacturers have sometimes obtained undeserved patents on obvious variations of existing drugs, such as particular formulations or dosing schedules. Potential solutions include more thorough review of pharmaceutical patent applications to enforce existing standards, or elevation of standards to limit the patentability of changes that offer little therapeutic advantage—an old idea that deserves renewed attention.^{74,75}

Policy makers took a promising step toward enforcing existing standards in 2011 with the passage of the Leahy-Smith America Invents Act. The act created a mechanism called *inter partes* review that allows stakeholders to challenge patents much more quickly and less expensively before an administrative Patent Trial and Appeal Board (PTAB).⁷⁶ Generic manufacturers, as well as independent parties such as hedge fund manager Kyle Bass, have challenged many drug patents via *inter partes* review.⁷⁷

Efforts to promote competition in these ways are bound to meet resistance from incumbents. In 2017, for example, Allergan sought to place certain patents covering cyclosporine ophthalmic emulsion (Restasis) beyond the reach of *inter partes* review by assigning them to the Saint Regis Mohawk Tribe, which then moved to terminate the proceedings on the basis of tribal sovereign immunity.⁷⁸ The PTAB denied the motion, but no court has yet ruled definitively on whether sovereign immunity can be used in this manner. Even if the judiciary does not hold the tactic invalid, however, Congress has already considered revising the statute to prohibit similar conduct by future litigants⁷⁹—that is, if *inter partes* review survives a pending Supreme Court challenge to the constitutionality of the administrative review process.⁸⁰

Conclusion

The US prescription drug market is insufficiently competitive as a result of many factors. Imperfect information, mandatory coverage laws, and current drug substitution laws impair rational decision making by payers. Exclusivities like patents, some of which are improperly granted, protect brand-name drugs from competition. High entry costs, raw material shortages, and slow FDA review can discourage or delay generic entry.

Various policy options can increase the effectiveness of both inter-brand and brand/generic competition, but they require legislative or regulatory changes. Until such interventions occur, the US will be unlikely

to substantially reduce its current spending levels for prescription drugs.

ACKNOWLEDGMENT/DISCLAIMER

The work at PORTAL is supported by the Laura and John Arnold Foundation, with additional support from the Harvard Program in Therapeutic Science and the Engelberg Foundation. PORTAL has also received a grant from the Anthem Public Policy Institute. These organizations had no role in the development of this paper. Aaron Kesselheim also reports receiving grants from the Food and Drug Administration Office of Generic Drugs and Division of Health Communication for unrelated work (2013–16).

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Health Affairs

Policy Options Papers are produced under a partnership of *Health Affairs* with the generous support of the Commonwealth Fund and Memorial Sloan Kettering Cancer Center.

Cite as: "Policy Options Paper: Promoting Competition To Address Pharmaceutical Prices," *Health Affairs*, March 15, 2018. DOI: 10.1377/hpb20180116.967310

PRESCRIPTION DRUG PRICING

POLICY OPTIONS PAPER

MARCH 15, 2018

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Policy Strategies For Aligning Price And Value For Brand-Name Pharmaceuticals

ABSTRACT Systemic factors in the US health care system lead to greater pricing power for drug manufacturers than is the case in other countries. The result is higher prices that are often poorly aligned with the degree of added benefit for patients and the health system. To achieve the difficult balance between necessary incentives for innovation and affordability, many economists favor “value-based” pricing, in which the price for a new drug reflects an assessment of the comparative effectiveness of the drug compared to other available treatments. In this brief we explore the different varieties of value-based pricing, and we outline several measures through which drug competition may be increased, supported by regulatory steps and payment mechanisms to bring drug prices into greater alignment with their underlying clinical value.

A variety of institutional and regulatory factors inflate the price of brand-name drugs in the United States to levels beyond what competitive markets would generate. Around the world, patents and exclusivities for drug products are used to support innovation in biopharmaceuticals by reducing the competition a brand-name producer faces. In the US, patents are granted by the US Patent Office for twenty years, and exclusivity periods are granted by the Food and Drug Administration (FDA) for three to seven years for small-molecule drugs and twelve years for biologics.

Higher incomes in the US ought to drive drug prices somewhat higher than in most other countries because of price elasticity in the market.^{1,2} However, several distinctive institutional and regulatory factors in the US help drive drug prices significantly higher than in other countries. First, half of Americans obtain drug coverage from tax-preferred employer-provided plans.³ This results in a distortion that funnels compensation toward more generous health plans, which in turn means that pharmaceutical manufacturers receive an inflated signal of demand. Similarly, Medicare is mostly funded by general revenues, so current recipients don't pay the full actuarial value of their prescription drug coverage, leading again to a relatively unconstrained signal of demand.

Second, insurers in the US are extremely permissive regarding the drugs for which they pay, and Medicare is prohibited from negotiating prices directly with manufacturers.⁴ While Medicare can decline to cover physician-administered drugs (under Part B) that are “not reasonable and necessary for the diagnosis or treatment of illness or injury,”⁵ the program has interpreted that language as preventing it from considering prices in coverage decisions. Medicare outpatient prescription drug coverage (under Part D) also has statutory language

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that requires broad coverage.⁶ Since private insurers generally follow Medicare's lead on coverage determinations, Medicare's permissiveness sets an implicit standard for all insurers.⁷

A third source of inflated demand for physician-administered drugs comes from the way in which physicians are reimbursed under Medicare Part B. They are paid each drug's average sales price plus 6 percent.⁸ This "cost-plus" payment method, often mirrored in contracts with private insurers, means that physicians have incentives to prescribe higher-price drugs. These incentives particularly affect oncologists, ophthalmologists, and rheumatologists, for whom the dispensation of Part B drugs is a large source of income.⁹

While drug prices for new products are high around the world because of patents and exclusivity periods,

future. However, competitive market forces can moderate pharmaceutical manufacturers' power to price treatments higher than their intrinsic clinical value.

ACCELERATED APPROVAL OF COMPETITORS

One competition-enhancing policy change would be to speed up the approval process for drugs that are potential competitors. In addition, federal regulators could take two steps to prevent delays in the introduction of generic versions of branded drugs. First, they could curb frivolous citizen petitions regarding safety concerns.¹⁰ Second, they could prohibit manipulation of Risk Evaluation and Mitigation Strategy processes. Under such processes, brand-name drug manufacturers often claim patient safety concerns in refusing to provide samples of their drugs to prospective generic manufacturers, who need them to demonstrate their version's equivalence.¹¹

CONTINGENT EXCLUSIVITY PERIODS

A more aggressive approach to enhancing competitive leverage over new branded drugs would be for Congress to make the length of exclusivity contingent on "reasonable" pricing behavior. Health economists frequently estimate a reasonable "value-based" price for a drug by applying a set ratio for increased pricing to the amount of health gain provided by the drug over other available treatments. This gain is usually measured in "quality-adjusted life years" (QALYs), which can be augmented by incorporating broader considerations such as impact on productivity.¹² The QALY has been criticized as inadequate to capture the full range of health benefits for some conditions, and it has at times been singled out for exclusion from application to coverage decisions by Medicare. However, the QALY retains the support of leading health economists and policy makers in the US and internationally as the best single combined measure of the health effects of any health care intervention.^{13,14}

To link reasonable pricing to the length of exclusivity, one option would be to leave manufacturers free to charge what they wanted but vary the length of their monopoly protection based on whether the resulting "cost per QALY," when combined with other demonstrated benefits, was deemed reasonable. For example, if the cost per QALY were between \$50,000 and \$150,000, a range frequently viewed by economists as reflecting intermediate value in the US,¹⁵ exclusiv-

“Institutional and regulatory factors drive US drug prices higher than in other countries.”

our thesis is that in the US, prices are even higher because of these three factors. This brief explores measures that could increase competitive market forces or apply new forms of regulatory oversight to put downward pressure on drug pricing in the US. These measures have a common purpose: to create a future in which the prices for brand-name drugs provide ample incentives for meaningful innovation but are determined more by their demonstrated value to patients than by factors that artificially inflate demand and magnify manufacturers' pricing power. The measures we describe are divided into those that improve competition for brand-name drugs and those that align pricing with comparative effectiveness.

■ Using Competition To Align Price With Value

The insurance and tax-related causes of inflated demand for pharmaceuticals will likely remain features of the US health care system for the foreseeable

ity for biologics could remain at the current twelve years. However, if the cost per QALY was lower than \$50,000, reflecting higher value, exclusivity could be increased to fifteen years. And if manufacturers were to choose a price such that the cost per QALY exceeds \$150,000, as is currently the case with many recent cancer drugs and other specialty pharmaceuticals, the exclusivity period could be set at seven years. If this kind of sliding scale were implemented, drugs would be more affordable, especially in the short term, but manufacturer profits could actually be higher in the long run because generic competition would be put off for longer (meaning that prices would be lower than at present but would remain higher than prices after generic entry).¹⁶ Contingent exclusivity would also encourage the development of drugs with higher QALYs, to permit higher pricing.

REIMPORTATION

Another option to improve branded drug competition is reimportation from other countries. Politicians from both parties have suggested allowing Americans to purchase drugs abroad.¹⁷ A prominent state policy think tank has recently drafted model legislation to permit widespread reimportation to be implemented legally and safely by states.¹⁸ However, most economists do not support reimportation, since drug manufacturers would likely react by raising prices, limiting supplies abroad, or both. Nonetheless, just the threat of reimportation might spur US manufacturers to exercise greater restraint and price their drugs more in alignment with clinical value.

Using Comparative Effectiveness To Align Price With Value

Stronger competitive market forces may help address some of the factors that cause US drug prices to be so much higher than in other countries. However, many experts believe that further measures will be necessary to create a pharmaceutical market in which prices more reliably reflect clinical value.^{19,20} One frequently mentioned approach is the application of comparative effectiveness information to guide pricing and coverage.²⁰

NEGOTIATION AND VALUE-BASED BENCHMARKS

As the largest payer in the US health care system, the federal government could follow the lead of all other industrialized countries in using comparative effectiveness research to negotiate coverage and pricing terms. In these countries, available evidence is used to estimate the relative benefits of a new drug compared to other treatments, and this comparison is used to scale the price of the new drug accordingly. There are two basic methods for doing this reliably across different types of treatments: linking pricing to different qualitative categories of comparative clinical effectiveness; and using a cost-effectiveness approach to calculate health gain quantitatively on a continuous scale and then assigning a proportional higher price per unit of added health gain.

France and Germany have long used categorical comparative effectiveness as the cornerstone of their national drug evaluation programs.^{21,22} In these systems, a governmental agency evaluates the evidence on the overall clinical benefits and side effects of a drug compared to the evidence for the other best treatment options. The comparative clinical effectiveness of the drug is then assigned to one of three or more categories, such as “no added benefit,” “minimal benefit,” or “substantial benefit.” These are qualitative judgments, not quantitative metrics. Drugs deemed to provide no added benefit receive a default price no higher than the lowest-price equivalently effective option, an approach commonly known as reference pricing. For drugs with some added benefit, price negotiation proceeds behind closed doors, often using prices from the UK and other European markets as benchmarks, but with the general assumption that the price for a new drug should reflect the underlying magnitude of its added clinical benefit.

The other option for scaling drug prices to their relative clinical benefits is to use cost-effectiveness techniques. The UK and Australia are best known for this approach, and when Germany, France, and other countries benchmark their prices to UK prices, they are, in effect, adopting the same underlying methodology. To make an “apples to apples” comparison among different drugs, the health effects are frequently combined to produce the QALY as a measure of overall health gain. If a new drug is shown to produce more QALYs than an alternative course of

treatment, a cost-effectiveness analysis will be able to estimate at what additional cost that clinical gain would be achieved at different price ranges for the new drug.

The final step in linking cost-effectiveness to the estimation of a value-based price for a drug involves a difficult question: Given other spending needs, how much should society be willing to spend for an average gain of one additional QALY, whether that added QALY comes from longer lives for patients with cancer, improved mental health for patients with

spending based on overall budgets and expected cost growth.²⁵ If drug costs exceed this cap, the state may use external value assessment reports to determine value-based price targets for key drugs. The state may then seek supplemental rebates to achieve these price targets, applying penalties to manufacturers that fail to negotiate to within 75 percent of the rebate needed to arrive at the value-based price. Although this program is in its early stages, the state has already announced that drug spending in 2018 is expected to exceed the spending cap, and therefore the first round of value-based price targets can be expected in the coming months.

INDICATION-SPECIFIC PRICING

Indication-specific pricing (ISP) for drugs used to treat multiple conditions is a potential way to apply the principles of value-based pricing.^{26,27} ISP can help reflect the variability in clinical value of a drug that has different relative benefits when used for different indications—such as a drug that extends life for many months when used to treat lung cancer but only several weeks when used for pancreatic cancer. For this drug, ISP would assign a higher price when prescribed for lung cancer and a lower price when used for pancreatic cancer.

Where ISP has been used outside the US, the multiple prices are usually not administered separately but are achieved indirectly by calculating a single “weighted average” price based on estimates of how many patients will use the drug for each of the different indications. Even this simplified approach to ISP is challenging in the US drug pricing system, which has a history of assigning a single price to a drug, no matter how it is used. There are also multiple administrative and regulatory challenges that currently darken the prospects for ISP in the US.²⁶ Nonetheless, ISP may be welcomed by manufacturers and payers because it offers the flexibility to price drugs lower for lower-value indications, and thereby help manufacturers gain market share without undermining higher prices for high-value indications. Interest in ISP has been catalyzed in the US, in part, by the announcement by Express Scripts that in 2016 it would launch an ISP initiative for certain cancer drugs. The details and outcomes of this program are not yet available.²⁶

“Competition can moderate manufacturers’ power to price drugs higher than their intrinsic clinical value.”

depression, or improvements in outcomes in any other health condition? Many health economists believe that the most appropriate answer for the US today lies somewhere between \$100,000 and \$150,000 per QALY.¹⁵ This range is used by the Institute of Clinical and Economic Review (ICER) in the calculation of its value-based price benchmarks, which have been the subject of extensive policy consideration and debate.^{23,24}

Any attempt to capture and quantify quality of life, and to place a dollar figure on the amount society should pay for added health, raises philosophical questions that translate into thorny political debates. Nonetheless, this approach has the merit of being more explicit and transparent than other negotiating schemes. The basic methods of cost-effectiveness have achieved broad consensus among health economists around the world and are the bedrock of discussions about aligning drug prices with their relative value for patients.

TARGETED, VALUE-BASED REBATES

Although proposals for Medicare to negotiate drug prices (with or without value-based price targets) have languished, some states are moving ahead with related initiatives. In New York, a 2017 law gives the state power to determine a cap for Medicaid drug

OUTCOMES-BASED AGREEMENTS

There are a growing number of agreements between manufacturers and payers in which the manufacturer will give an enhanced rebate, or even a full refund, when the drug is ineffective in some way. In one

“The US could follow other industrialized countries, using comparative effectiveness to negotiate prices.”

prominent example, Amgen pays a greater rebate to Harvard Pilgrim Health Care whenever its drug for treating high cholesterol fails to prevent a patient from suffering a stroke or heart attack.²⁸

However, while outcomes-based contracts do link the effective price for a drug with patient outcomes, this should not be confused with true value-based pricing. A small refund, as the Harvard Pilgrim–Amgen deal provides, does not address whether the initial price, or the effective price after all rebates, is aligned reasonably with the added clinical benefit. Outcomes-based contracting offers an attractive way to link pricing to clinical value, and it has great potential—but only if it can be scaled appropriately. If not, it may even risk diverting attention from the larger goal of linking drug prices in a reasonable and proportional way to their relative added benefits for patients.

Conclusion

We began by noting that a raft of systemic factors in the US magnify the protections provided by patents and exclusivity periods, leading to drug prices higher than the point at which affordability is balanced with the rewards necessary for innovation. This insight suggests that efforts to constrain prices by aligning them with clinical value would not stifle innovation. In fact, measures to enhance competitive market forces and to leverage comparative effectiveness to achieve value-based pricing would provide more explicit incentives for the kind of innovation that should be rewarded handsomely within the US health care system. The innovation that “wins” when prices align with clinical value is the innovation that demonstrates its ability to improve the lives of patients.

But savings for purchasers or patients from value-based pricing mean revenue lost for some manufacturers, whose will to fight to retain those revenues should not be underestimated. Medicare is the leading payer for cancer drugs, whose prices have risen faster than any other segment of the pharmaceutical industry.²⁹ Hoped-for future treatments of Alzheimer disease will almost certainly be paid for by Medicare, while Medicaid is likely to be the leading payer for the coming wave of gene therapies for rare pediatric conditions. To address the current crisis in affordability for many drugs while establishing a more sustainable model for innovation in the future, now is the time to invest in federal efforts to align drug prices with clinical value.

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Policy Options Papers are produced under a partnership of *Health Affairs* with the generous support of the Commonwealth Fund and Memorial Sloan Kettering Cancer Center.

Cite as: "Policy Options Paper: Policy Strategies For Aligning Price And Value For Brand-Name Pharmaceuticals," *Health Affairs*, March 15, 2018. DOI: 10.1377/hpb20180216.92303.

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