Promoting Competition in Drug Pricing: A Review of Recent Congressional Legislation

Health Policy Portal

Sarosh Nagar and Aaron S. Kesselheim

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Abstract: Brand-name prescription drug manufacturers use various strategies to extend their market exclusivity periods by delaying generic or biosimilar competition. Recent Congressional legislation has targeted four such tactics. We analyze these proposals and assess their likely effect on competition in the U.S. drug market.

Drug prices for brand-name medications in the U.S. are substantially higher than in comparable industrialized nations.[1] Spending on brand-name drugs also accounts for a majority of total American drug spending.[2] High prices are facilitated by market exclusivity periods that begin after FDA approval, during which time patents and other statutory protections shield the approved drug from direct competition.[3] Prices only predictably fall after the end of the market exclusivity period and the entry of competitor generic or biosimilar drugs.[4]

Delays to generic or biosimilar entry have therefore been very profitable to drug manufacturers. Examples of strategies brand-name manufacturers have used or tried to use in recent years to block generic entry include obtaining dozens of patents protecting their drug product and transferring the patent rights to a Native American tribe to undermine patent challenges.[5] In October 2021, the U.S. House of Representatives evaluated some new pieces of legislation seeking to address four competition-delaying tactics: reverse payment settlements, product hopping, sham petitions, and the patent dance. In this article, we explain how these tactics work, review the design of the legislative proposals seeking to address these practices, and assess the likelihood that these proposals, if enacted, would effectively promote timely competition in the US drug market.

Product Hopping

Product hopping refers to the practice in which brand-name drug manufacturers switch from selling an established version of their drug to a new formulation that has existing patents or other market exclusivities.[6] Product hopping is often timed strategically to occur in the year or two before generics are about to enter so that the brand-name manufacturer can retain a revenue stream from a subset of patients. It is most problematic when the new formulation offers no effectiveness or safety advantages over the original version.

A classic example of product hopping was the introduction of proton-pump inhibitor esomeprazole (Nexium) by AstraZeneca as the market exclusivity for its original blockbuster "purple pill" proton-pump inhibitor omeprazole (Prilosec) was ending.[7] Esomeprazole was the single-enantiomer formulation of the racemic omeprazole, and it had no clinical

Sarosh Nagar *is from the Program On Regulation, Therapeutics, And Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School.* **Aaron S. Kesselheim, M.D., J.D., M.P.H.,** *is Director of the Program On Regulation, Therapeutics, And Law (PORTAL), Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School.*

About This Column

Aaron Kesselheim serves as the editor for Health Policy Portal. Dr. Kesselheim is the *JLME* editor-in-chief and director of the Program On Regulation, Therapeutics, And Law at Brigham and Women's Hospital/Harvard Medical School. This column features timely analyses and perspectives on issues at the intersection of medicine, law, and health policy that are directly relevant to patient care. If you would like to submit to this section of *JLME*, please contact Dr. Kesselheim at akesselheim@bwh.harvard.edu.

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benefits at equivalent doses. A more recent example involved the opioid use disorder (OUD) drug buprenorphine/naloxone (Suboxone), in which the drug's manufacturer, Reckitt Benckiser, introduced a sublingual film as the exclusivity on the original tablet formulation of the drug was expiring.[8] Reckitt Benckiser then began publicizing the possibility of safety concerns about the original tablet formulation to promote sales of the follow-on product.[9]

Product-hopping can involve a "hard switch" in which a manufacturer discontinues the original drug in favor of the follow-on product or a "soft switch" in which both drugs remain on the market, but only the follow-on drug is marketed.[10] An example of an attempted hard switch occurred with the Alzheimer's drug memantine (Namenda), a twice-daily formulation, in which the drug's manufacturer, Forest Laboratories, attempted to discontinue the sale of memantine at the end of its market exclusivity period in favor of memantine XR, a once-daily formulation.[11] Memantine XR had no clinical benefits (other than convenience) over memantine, but the follow-on product had about a decade of additional market exclusivity left after the original memantine's exclusivity expired.[12] The case of esomeprazole and omeprazole is an example of a soft switch, as, unlike memantine, omeprazole remained on the market even after it lost market exclusivity, but AstraZeneca stopped advertising the original prescription formulation of omeprazole and instead promoted the follow-on esomeprazole as "the new purple pill."[13]

H.R. 2873, the Affordable Prescriptions for Patients Through Promoting Competition Act of 2021, was introduced by Rep. David Cicilline (D-RI) to address product hopping. The bill classifies both hard switch and soft switch product hopping as potentially illegal anticompetitive behavior and permits the Federal Trade Commission (FTC) to initiate litigation or impose administrative penalties on manufacturers engaging in illegal product-hopping. The bill specifies that switches for certain clearly legitimate reasons like safety or supply are exempted from being classified as product hopping.[14]

Sham Citizen Petitions

The FDA permits American consumers to file so-called citizen petitions to request changes to health care regulations.[15] Brand-name drug manufacturers, however, have been found to frequently use this pathway to petition for delayed entry of generic medications, claiming that the generic is non-substitutable or even dangerous.[16] While some of these petitions express legitimate concerns, so-called sham petitions allege without reasonable scientific basis that generic medications are unsafe and require further testing.[17] From 2011-2015, 124 citizen petitions relating to generic applications were filed, with 87% arising from brand-name manufacturers (92% were ultimately denied).[18] Their adjudication can cause substantial delays to generic approval (of up to 150 days per petition, according to one report), and thus petitions extend market exclusivity for high-priced brand-name drugs.[19]

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One prominent example of a questionable citizen petition involves the brand-name opioid use disorder (OUD) drug buprenorphine (Subutex).[20] When buprenorphine's market exclusivity was close to expiring, the drug's manufacturer, Reckitt Benckiser, filed citizen petitions requesting the FDA take action and block the sale of generic buprenorphine.[21] The petition was filed on the grounds that the generic drug's packaging was not as child-safe as the packing of the reference product.[22] The FDA denied the petition, but the adjudication process delayed the market entry of generic buprenorphine. Other examples of potentially problematic petitions include one filed by Mutual Pharmaceuticals to delay the entry of generic competitors to their blood pressure medication felodipine (Plendil), in which Mutual alleged that the generic competitor drug negatively impacted a patient's ability to digest a certain variety of orange juice.[23] This petition was also denied by the FDA, but only after delaying generic market entry.

In Congress, Rep. Hakeem Jeffries (D-NY) introduced H.R. 2883, the Stop Stalling Access to Affordable Medications Act, to help prevent frivolous petitions. The bill classifies "sham" petitions as a violation of antitrust law and permits the Secretary of Health and Human Services to label citizen petitions as such if evidence suggests that a brand-name drug manufacturer filed the petition to delay generic entry, such as if petitions coincided temporally with the filing of a generic drug's approval application. The Federal Trade Com-

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mission (FTC) can then sue the drug manufacturer that filed the petition to seek civil relief.[24]

Reverse Payment Settlements

The 1984 Hatch-Waxman Act, which defined the process for regulatory approval of generic drugs, created a mechanism to adjudicate brand-name manufacturers' drug patents leading up to generic entry. In brief, generic manufacturer must certify that they are entering a market not protected by patents, or that their products do not infringe brand-name manufacturers' patents or that those patents are invalid. If the brand-name manufacturer disagrees as to existing patents, it can file a claim, leading to a lawsuit.[25] These lawsuits are critical for public health, because they can clear out weak or improperly granted patents that block entry of lower-cost generic drugs (or, alternatively, allow manufacturers to enforce their valid intellectual property against competitors).[26] However, many of these lawsuits end with settlements, some of which include direct financial payments from the brand-name to the generic challenger.[27] When such settlements prop up patents that would have been invalidated, they extend a brand-name drug's market exclusivity and allow prices to remain high. A classic example of a so-called "reverse payment settlement" (called such because the patent holder is paying the patent challenger as part of the settlement, rather than the more normal opposite situation) is the case of narcolepsy drug modafinil (Provigil), in which the drug's manufacturer, Cephalon, resolved a patent infringement case in part by paying generic manufacturers $300 million in exchange for which the generic agreed to delay market entry for six years.[28]

The Hatch-Waxman Act litigation patent settlement landscape changed about a decade ago with a Supreme Court case involving patents related to testosterone gel (Androgel). In 2003, the period of market exclusivity for Solvay Pharmaceuticals' topical testosterone gel neared expiry, prompting Actavis to file for approval of a competitor generic. To maintain market exclusivity, Solvay filed a patent infringement claim against Actavis as part of the Hatch-Waxman process. When the resulting challenge was settled, Actavis agreed to delay the market entry of its generic in exchange for an annual payment of up to $30 million dollars from Solvay for nine years. The Federal Trade Commission (FTC) alleged this agreement was anticompetitive and sued Actavis.[29] In *FTC v. Actavis,* the Supreme Court held that reverse payment settlements could be challenged on antitrust grounds if they unreasonably restricted market competition.[30] *FTC v. Actavis* thus opened the door to legal scrutiny of reverse payment settlements, resulting in a substantial decline in the prevalence of reverse payment settlements.[31] While settlements have continued, they have tended to avoid direct payments and instead brand-name and generic manufacturers have developed alternative arrangements.[32] For example, in no-authorized generic agreements, generic companies agree to delay market entry of their product in exchange for brand-name manufacturers agreeing not to authorize or make their own generic drugs in the future.[33] The generic manufacturer is functionally "paid" to delay generic market entry with a legal guarantee that their generic product will face less possible competition in the future.[34]

H.R. 2891, the Preserve Access to Affordable Generics and Biosimilars Act, was introduced by Rep. Jerrold Nadler (D-NY) to combat reverse payment settlements. H.R. 2891 bans legal settlements that delay the market entry of generic competitor medications in exchange for any form of compensation, whether a direct payment, royalty, or in any other item. It allows the FTC to initiate civil proceedings against manufacturers that sign such settlements. The only settlements permitted under H.R. 2891 are agreements unrelated to generic entry or with pro-competitive effects.[35]

Biosimilar Competition

The 2009 Biologics Price Competition and Innovation Act (BPCIA) created an expedited entry process for competition in the biologic drug market via biosimilar drugs, versions of biologics made by other manufacturers. In place of the patent listing and litigation procedure in the Hatch-Waxman Act, the BPCIA created a "patent dance" in which prospective biosimilar manufacturers must submit a copy of their regulatory approval application to the originator biologic manufacturer.[36] The originator manufacturer then provides a list of patents on which it claims the biosimilar infringes within 60 days, which eventually leads to litigation. This "dance" of information exchanges occurs fully outside of the public eye and may last for hundreds of days and still end in drawn-out litigation.[37] For example, in 2019, Hospira attempted to introduce a biosimilar to Amgen's anemia drug epoetin (Epogen).[38] Amgen reportedly dragged out the dance, leading to a delay in the approval of the biosimilar.[39]

Because the patent dance can lead to delays and because biosimilar manufacturers may not be comfortable revealing business information contained in their regulatory application to their competitors, some biosimilar manufacturers have skipped the patent dance. Sandoz introduced a biosimilar to Amgen's cancer drug filgrastim (Neupogen), but refused to follow through with the dance.[40] After Amgen sued Sandoz, the Supreme Court ruled in 2017 that the patent dance was not mandatory.[41]

H.R. 2884, the Affordable Prescriptions for Patients Through Improvements to Patent Litigation Act, was introduced by Rep. Henry Johnson (D-GA) to improve the patent dance. The bill redefines "patent infringement" to refer to solely those patents that infringe on claims on a biological product or the products or methods used in its manufacturing. The bill sets a limit of 20 patents that biologic manufacturers can reference in patent infringement claims during the patent dance and requires that these patents fit certain criteria for recency and importance. However, H.R. 2884 also permits manufacturers to supersede these limitations if courts deem the consideration of certain excluded patents to be important.[42]

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Discussion

Of the four bills, H.R. 2884 is likely to have the smallest impact on drug prices. While the biosimilar entry process as designed in the BPCIA can significantly delay the entry of competitor biosimilars, H.R. 2884 only limits the number of patents included in the dance, rather than limiting the amount of time allocated for each step in the so-called patent dance.[43] Hence, even with a limited number of patent infringement claims, brand-name drug manufacturers may still attempt to delay their responses and slow the process to delay biosimilar entry. The degree to which courts may grant exemptions to H.R. 2884's patent limitations further creates uncertainty about the bill's ability to hasten biosimilar market entry and lower drug prices.

H.R. 2883 on citizen petitions is more tangentially related to drug prices. In the past, the FTC has lost cases in which it alleged citizen petition abuse, such as in the 2019 case *FTC v. ShireViroPharma* in the Third Circuit Court of Appeals, because it has previously been unclear whether frivolous citizen petitions constitute violations of antitrust law.[44] H.R. 2883 resolves this problem by classifying frivolous petitions as illegal and anticompetitive behavior. However, H.R. 2883 relies on HHS to designate instances of frivolous petitions against which the FTC may litigate, and therefore requires HHS to be aggressive in making these designations. In 2007, Congress gave HHS and the FDA the ability to identify and summarily deny frivolous petitions without lengthy adjudication periods, but for the next seven years, the FDA did not summarily deny a single petition, despite hundreds of petitions being filed, many of limited merit.[45] If FDA and HHS continue to be reticent to aggressively identify and act against frivolous petitions, it may limit the effectiveness of H.R. 2883.

H.R. 2891, on reverse payment settlements, is likely to have a more substantial impact on hastening generic entry and lowering prices. H.R. 2891 bans settlements in which brand-name manufacturers pay or compensate generic manufacturers in some form to delay competitor generic drug market entry.[46] Therefore, H.R. 2891 blocks both traditional reverse-payment settlements and may extend to other alternative settlements such as no-authorized generic agreements. As a result, H.R. 2891 would broadly curb the use of settlements as a tactic to delay generic entry. However, whether that result would translate directly into lower drug prices remains to be seen, as in the post-*Actavis* era, the number of settlements involving direct payments has declined as many manufacturers have already switched to using more FTC-friendly settlements to avoid legal scrutiny.[47]

H.R. 2873 on product hopping may also have an important effect on drug prices. Currently, legal efforts to block product hopping have been stymied by inconsistent definitions of product hopping and uncertainty over whether it can constitute anticompetitive behavior.[48] H.R. 2873 provides standard definitions of both hard-switch and soft-switch product hopping and classifying both actions as potentially anticompetitive.[49] The clear definitions and legal grounds give the FTC more support in initiating litigation against parties engaged in problematic product hopping. Since the FTC has historically been aggressive in countering tactics that delay generic entry, it is likely the agency would vigorously enforce H.R. 2873. In turn, this enforcement would prevent brand-name manufacturers from extending market exclusivity and lead to lower drug prices.

Conclusion

The four bills introduced into Congress may have varying levels of effectiveness in hastening generic drug entry and lowering drug prices. To supplement these efforts to lower drug prices, Congress should adopt other measures, such as permitting Medicare and other insurers to negotiate brand-name drug prices or implement value-based pricing (VBP) and health technology assessment (HTA) standards to help ensure a drug's price is more closely related to its therapeutic benefits. These reforms would help lower the price of existing brand-name drugs, and combined with efforts to promote generic competition included in these four bills, would promote pharmaceutical competition and innovation for the benefit of patients.

Note

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