USING THE INFLATION REDUCTION ACT TO REIN IN PATENTING & EVERGREENING ABUSES

By Jishian Ravinthiran

December 11, 2024

PUBLICCITIZEN

ACKNOWLEDGMENTS

This report was written by Jishian Ravinthiran, a researcher in Public Citizen's Access to Medicine's Program. Steve Knievel and Peter Maybarduk, advocate and director of the Access to Medicines Program respectively, edited the report. Research and writing assistance were provided by Bryce Robinson, a legal intern with the Access to Medicines Program. We are very grateful for the thoughts and feedback received from Alex Moss, executive director of the Public Interest Patent Law Institute, and Tahir Amin, CEO of the Initiative for Medicines, Access, and Knowledge (I-MAK).

ABOUT PUBLIC CITIZEN

Public Citizen is a national non-profit organization with more than 500,000 members and supporters. We represent consumer interests through lobbying, litigation, administrative advocacy, research, and public education on a broad range of issues including consumer rights in the marketplace, product safety, financial regulation, worker safety, safe and affordable health care, campaign finance reform and government ethics, fair trade, climate change, and corporate and government accountability.

Contact Public Citizen

Main Office	Capitol Hill	Texas Office
1600 20th St. NW Washington, DC 20009	215 Pennsylvania Ave. SE, #3 Washington, DC 20003	309 E. 11th St., Suite 2 Austin, TX 78701
Phone: (202) 588-1000	Phone: (202) 546-4996	Phone: (512) 477-1155

For more information, please visit www.citizen.org.

Contents

KEY FINDINGS

Under the Inflation Reduction Act (IRA), the Centers for Medicare and Medicaid Services (CMS) now has the ability to negotiate maximum fair prices of select drugs for Medicare beneficiaries for the first time in the program's history.[1] With this new authority, CMS can resist the excessively high prices of the pharmaceutical industry and deliver lower out-of-pocket costs for Medicare beneficiaries, many of whom pay hundreds of dollars, if not thousands, for a single essential medication. In negotiating these prices, Public Citizen urges CMS to account for patent abuses by manufacturers that enable price gouging on the drugs selected for Medicare price negotiation in the first place. Many of these patent abuses fall into the category of "evergreening tactics," which cover patenting trivial and/or obvious modifications of existing medications to lengthen exclusivity on branded medicines.[2] In this report, we analyze the patenting and evergreening abuses on the first 10 drugs selected for Medicare price negotiation.

- Four of the 10 drugs subject to negotiation would likely have faced competition before negotiated prices go into effect were it not for evergreening tactics and patent abuses. As a result, **Medicare will lose between $4.9 and $5.4 billion in savings** that should have accrued from access to competing, lower-cost treatments**. These lost savings are nearly as much as what Medicare is expected to save if negotiated prices go into effect on all of the selected drugs in the first year of the program ($6 billion).**[3]

- Evergreening practices were prevalent across the drugs selected for price negotiation. Nine out of 10 drugs subject to negotiation show evidence of manufacturers engaging in blatant anticompetitive uses of patents to fend off generic or biosimilar competitors or evergreening abuses representing minor modifications or tweaks that unfairly lengthen monopoly protection on the drugs. Patent protection on the branded drugs could extend well into the 2030s and possibly 2040.

- Manufacturers of Eliquis, Imbruvica, Jardiance, Farxiga, and Entresto obtained patents on obvious or minor variations of earlier patent claims, such as crystalline forms of drug compounds which would be discovered and managed during

[1] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023), https://www.whitehouse.gov/briefing-room/statements-releases/2023/08/29/fact-sheet-biden-harris-administration-announces-first-ten-drugs-selected-for-medicare-price-negotiation/.
[2] Robin Feldman, *Understanding 'Evergreening': Making Minor Modifications Of Existing Medications To Extend Protections*, 41 HEALTH AFF. 801 (2022), https://www.healthaffairs.org/doi/10.1377/hlthaff.2022.00374.
[3] Ctrs. Medicare & Medicaid Servs., Fact Sheet: Medicare Drug Price Negotiation Program: Negotiated Prices for Initial Price Applicability Year 2026 (Aug. 14, 2024), https://www.cms.gov/newsroom/fact-sheets/medicare-drug-price-negotiation-program-negotiated-prices-initial-price-applicability-year-2026.

routine testing that is part of the drug approval process. These patents allow manufacturers to expand or extend monopoly control on these drugs.

- Manufacturers of Januvia, Stelara, Xarelto, Imbruvica, Jardiance, and Farxiga have obtained patents by relying on previously known information that was publicly available or disclosed in prior patents to extend monopoly control on the branded medications. For example, later patents claimed particular salt forms and methods of using drugs (1) disclosed or claimed in earlier patents, or (2) previously disclosed in publicly available summaries of clinical studies conducted using those drugs.

- Manufacturers of Stelara, Enbrel, and Jardiance engaged in blatant anticompetitive uses of patents, such as (1) using recently acquired patents that have nothing to do with producing a branded drug to block competing products, (2) exploiting deceitful licensing arrangements to maintain duplicative protection on branded medicines, and (3) patenting methods of ensuring patient safety and therapeutic efficacy prior to treatment.

- The evergreening tactics and patent abuses documented here suggest Congress should advance laws that curtail gaming the patent system to the detriment of U.S. patients. While the Affordable Prescriptions for Patients Act of 2023, passed by the Senate, is a step in the right direction, the PREVAIL Act sponsored by Senators Chris Coons and Thom Tillis could be devastating for patient access by making it harder for generic and biosimilar manufacturers and nonprofit organizations to administratively challenge branded drugmakers' patent abuses.

INTRODUCTION

The Inflation Reduction Act (IRA) is a significant step towards taming drug pricing abuses and providing affordable access to essential medications for Medicare beneficiaries. For the first time in its nearly 20-year history, Medicare can negotiate prices with pharmaceutical companies for selected drugs, instead of accepting industry's excessively high prices.[4] The first ten drugs selected for price negotiation cost Medicare anywhere between $2.5 billion to $16 billion a year, imposing hundreds of dollars and sometimes thousands of dollars in out-of-pocket costs on patients.[5] In negotiating maximum fair prices for enrollees, CMS considers a number of factors within statutorily prescribed ceilings, including the patents on the drug.[6]

Public Citizen urges CMS to account for patent abuses by manufacturers that enable price gouging on the drugs selected for Medicare price negotiation. As discussed in our analysis below, nine of the ten drugs subject to negotiation demonstrate evidence of patenting tactics designed to unfairly lengthen monopoly protections on the drugs to the detriment of American patients. Many of these practices are often called "evergreening abuses," which cover patenting trivial and/or obvious modifications of existing medications to lengthen exclusivity on branded medicines.[7] Lower-cost alternatives have already launched abroad for many of the drugs subject to negotiation because the American patent system provides, at times, greater leniency in granting patents on these minor modifications. Thus, CMS should consider how patents and exclusivities in the United States unfairly delay and/or prevent access to more affordable treatment options for Medicare beneficiaries.

First, we underscore that four of the ten drugs subject to negotiation would likely have faced competition before negotiated prices go into effect were it not for discrete patenting abuses or evergreening tactics. As a result, **Medicare will lose approximately five billion dollars in savings** that should have accrued from access to competing, lower-cost treatments. We strongly urge CMS to consider the massive losses to Medicare and taxpayers that arise from patent abuses on drugs subject to future rounds of negotiation and renegotiation.

---

[4] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023), https://www.whitehouse.gov/briefing-room/statements-releases/2023/08/29/fact-sheet-biden-harris-administration-announces-first-ten-drugs-selected-for-medicare-price-negotiation/.

[5] *Id*. Out-of-pocket costs for enrollees without the low-income subsidy are detailed in subsequent sections.

[6] Memorandum from Meena Seshamani, Deputy Administrator, Ctrs. Medicare & Medicaid Servs., to Interested Parties, Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026 Medicare, at 130, 150-51 (June 30, 2023), https://www.cms.gov/files/document/revised-medicare-drug-price-negotiation-program-guidance-june-2023.pdf.

[7] Robin Feldman, *Understanding 'Evergreening': Making Minor Modifications Of Existing Medications To Extend Protections*, 41 HEALTH AFF. 801 (2022), https://www.healthaffairs.org/doi/10.1377/hlthaff.2022.00374.

Second, we provide a description of the patenting tactics manufacturers have used to unfairly extend patent protection on eight of the ten drugs selected for negotiation. Fiasp and Novolog are already off patent, so we do not analyze patenting practices on these drugs. In a prior report, we had already detailed the deceitful contracting practices Amgen used to maintain duplicative protection over etanercept (marketed as Enbrel) that extends exclusivity by an additional decade after patent protection in the drug was set to expire in 2019.[8] We briefly summarize that report here; but through additional analysis of the drugs selected for price negotiation, we find that manufacturers often obtain patents on obvious or minor variations of earlier patent claims. These variations are obvious or minor because of (1) standard processes for screening compounds across the drug industry and (2) previously known information publicly available or disclosed in prior patents. In certain cases, we found blatant anticompetitive uses of patents such as (1) when companies use recently acquired patents that have nothing to do with producing a branded drug to block competing products and (2) when manufacturers potentially lengthen exclusivity by patenting methods of screening patients to ensure the drug's safety and efficacy.

The IRA's negotiation provisions finally deliver to the government a powerful tool to curb these kinds of abuses by the pharmaceutical industry. But its success in delivering taxpayers and consumers relief from excessive pricing by drug corporations demands fully recognizing the pricing impacts of inappropriate monopoly extensions. CMS must consider these unfair patenting practices and their significant financial consequences to patients and Medicare in evaluating patents and exclusivity data submitted by manufacturers. Future administrations must curb price gouging that arises from pervasive patenting abuses and unfairly extended monopoly control to ensure fair prices of selected drugs for Medicare and its enrollees.

[8] JISHIAN RAVINTHIRAN & STEVE KNIEVEL, USING THE INFLATION REDUCTION ACT TO REIN IN PHARMACEUTICAL COMPANY ABUSES: THE CASE OF ENBREL (2023).

PATENT ABUSES ON IRA DRUGS WILL COST TAXPAYERS NEARLY $5 BILLION BY 2026

According to our analyses (discussed in sections specific to each drug below), four of the ten drugs subject to Medicare price negotiation would likely have faced generic and biosimilar competition by the time negotiated prices go into effect on January 1, 2026, were it not for drug corporations' evergreening and patent abuses. **As a result, taxpayers will have lost between $4.9 and $5.4 billion by January 1, 2026 due to patenting practices that delay access and deprive Medicare enrollees of lower-cost alternatives to the drugs selected for price negotiation.**

In a previous report, we estimated that, because of Amgen's unfair patenting practices on Enbrel, Medicare will have lost $1,891,500,836 by January 1, 2026 due to the absence of biosimilar competition.[9] After examining the patenting practices for ustekinumab (marketed as Stelara), rivaroxaban (marketed as Xarelto), and sitagliptin (marketed as Januvia), we determined that the patent protection for these drugs would have expired before negotiated prices go into effect were it not for specific patent abuses and evergreened patents. We estimated lost savings to Medicare due to the absence of biosimilar and generic competition on these drugs and aggregated those estimates with our prior projection for lost savings to Medicare due to Amgen's patent abuses.

Stelara is a biologic drug. Biologics are different from chemically synthesized small molecule drugs, are generally larger and more complex, and are typically derived from living material.[10] A biosimilar product is a biological product which is highly similar to the original biologic and has no clinically meaningful differences.[11] Like generics for branded small molecule drugs, biosimilars are versions of brand name biologics and may provide more affordable treatment options to patients.[12] We estimate how much Medicare would have saved if Stelara faced biosimilar competition after patent protection was set to expire in September 2023 until January 2025, when the first biosimilar is set to enter the market.[13] Because of greater uncertainty in biosimilar uptake and price reductions

[9] JISHIAN RAVINTHIRAN & STEVE KNIEVEL, USING THE INFLATION REDUCTION ACT TO REIN IN PHARMACEUTICAL COMPANY ABUSES: THE CASE OF ENBREL 7 (2023).

[10] *Frequently Asked Questions About Therapeutic Biological Products*, U.S. FOOD & DRUG ADMIN. https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/frequently-asked-questions-about-therapeutic-biological-products#:~:text=In%20contrast%20to%20chemically%20synthesized,are%20usually%20not%20fully%20characterized (last visited Aug. 19, 2024).

[11] *Biological Products Definition*, U.S. FOOD & DRUG ADMIN. https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf (last visited Aug. 19, 2024).

[12] *Id*.

[13] Amended Complaint at 51-54, CareFirst of M.D. v. Johnson & Johnson, Civil Action No. 2:23-cv-00629-JKW-LRL (E.D. Va. Feb. 5, 2024), https://www.hbsslaw.com/sites/default/files/case-downloads/stelara-antitrust/2024-02-05-amended-complaint.pdf; *see also* Jonathan Gardner, *Acquired patents aid J&J defense of top-selling drug from biosimilar challenge*, BIOPHARMA DIVE (Mar. 29, 2023),

compared to the branded biologic, we provide a lower-bound and upper-bound estimate of lost savings to Medicare due to these patent abuses (*see* Appendix).

Under a more conservative set assumptions, we find that Medicare will likely lose at least $90,993,529.99 just on this one treatment due to patent abuses. Under more optimistic assumptions about the effect of biosimilar competition, Medicare may lose as much as $568,709,562.45 on Stelara by the time negotiated prices go into effect.

That is, if it were not for Johnson & Johnson's unfair patenting practices, Medicare beneficiaries would have had access to more affordable alternatives and taxpayers would have spent on a net basis approximately $91 million to $569 million less just on this one drug by the time negotiated prices go into effect.

Similarly, we estimated lost savings to Medicare as a result of evergreening practices on the two small molecule drugs, Januvia and Xarelto, that deprive Medicare beneficiaries of lower cost generics. We can estimate lost savings on these drugs with more certainty given currently available data (see Appendix).

If Xarelto faced generic competition after its patent protection was set to expire in May 2025, Medicare would have spent on a net basis $595,101,482.46 less just on this one drug by the time negotiated prices go into effect. Similarly, Medicare will have lost $2,334,949,973.16 due to Merck's evergreening practices on Januvia because patent protection in the drug would have otherwise expired in January 2023. **That is, the absence of generic competition on Xarelto and Januvia due to evergreening practices will cost Medicare over $2.9 billion by the time negotiated prices go into effect.**

In aggregate, corporations' patent abuses and evergreening practices on Stelara, Xarelto, Januvia, and Enbrel will deprive Medicare enrollees of more affordable alternatives and cost taxpayers **between $4.9 and $5.4 billion** by the time negotiated prices take effect. This underscores that CMS must account for patenting practices designed to unfairly lengthen monopoly control and resulting massive losses to Medicare and patients in establishing maximum fair prices for drugs subject to price negotiation.

https://www.biopharmadive.com/news/johnson-johnson-stelara-patents-amgen-biosimilar-momenta/646277/; Johnson & Johnson, 2021 Form 10-K at 3, https://www.sec.gov/ix?doc=/Archives/edgar/data/0000200406/000020040621000008/jnj-20210103.htm.

Table 1. Lost Savings to Medicare Due to Patenting Practices

Drug	Lost Savings to Medicare
Stelara	$91 - $569 million
Xarelto	$595 million
Januvia	$2.33 billion
Enbrel	$1.89 billion
Total	$4.9 - $5.4 billion

EVERGREENING & PATENT ABUSES ON THE IRA DRUGS

In this section, we describe the evergreening and patent abuses on eight of the 10 drugs selected for negotiation. An earlier report already focused on Amgen's patent gamesmanship on etanercept (marketed as Enbrel), which we have summarized at the end of this section.[14] Insulin aspart (marketed as Novolog and Fiasp) is already off-patent, but biosimilars have not reached the market yet due to data deficiencies and problems surfaced during inspections of manufacturing facilities.[15] Nine out of 10 drugs subject to negotiation show evidence of manufacturers engaging in blatant anticompetitive uses of patents to fend off generic or biosimilar competitors or evergreening abuses representing minor modifications or tweaks that unfairly lengthen monopoly protection on the drugs. This highlights that the Inflation Reduction Act must rein in pricing abuses based on this extended monopoly control that hurts American patients by depriving them of more affordable treatment options, which are often available much earlier to patients abroad.

Stelara (Ustekinumab)

Ustekinumab, marketed as Stelara by Johnson & Johnson, is a biologic that treats psoriasis, psoriatic arthritis, Crohn's disease, and ulcerative colitis.[16] Between June 2022 and May 2023, Medicare Part D spent $2.6 billion covering the cost of this medication for 22,000

[14] JISHIAN RAVINTHIRAN & STEVE KNIEVEL, USING THE INFLATION REDUCTION ACT TO REIN IN PHARMACEUTICAL COMPANY ABUSES: THE CASE OF ENBREL (2023).
[15] Kevin Dunleavy, *FDA rejects Biocon insulin biosimilar over data, manufacturing concerns*, FIERCE PHARMA (Jan. 12, 2023), https://www.fiercepharma.com/manufacturing/biocon-slapped-crl-its-novo-nordisk-insulin-biosimilar.
[16] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES: STELARA: MEDICARE ENROLLEE USE AND SPENDING (Nov. 9, 2023), https://aspe.hhs.gov/sites/default/files/documents/6c981fa9e709a299f72f5898e0205c20/Stelara.pdf.

enrollees, equating to roughly $120,00 per beneficiary.[17] Enrollees who did not receive the low-income subsidy paid on average $4,207 in out-of-pock costs annually to receive this drug.[18]

The FDA first approved Stelara in 2009 for treating patients with moderate to severe plaque psoriasis.[19] Since its approval fifteen years ago, Johnson & Johnson has reportedly earned over **$60 billion** in revenues from sales of the medication.[20] Experts, and even Johnson & Johnson, had estimated that the company would lose exclusivity over the drug in September 2023.[21] This aligns with the expiration date of the patent covering ustekinumab, the active ingredient of Stelara.[22] However, Johnson & Johnson engaged in patent abuses to extract settlements from biosimilar companies that delayed entry of competitors until January 2025 in the United States.[23] In contrast, biosimilars are already available to patients in Canada, Japan, and Europe.[24] To obtain longer monopoly protections in the United States, Johnson and Johnson asserted (1) acquired patents expiring in 2032 and 2033 which are not used in the manufacture of their product, purely for the anticompetitive purpose of blocking biosimilar competition, and (2) a method of use patent on ulcerative colitis expiring in 2039 claiming a previously disclosed therapeutic application.

---

[17] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).
[18] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES: STELARA: MEDICARE ENROLLEE USE AND SPENDING (Nov. 9, 2023).
[19] *Biologic License Application (BLA): 125261*, U.S. FOOD & DRUG ADMIN., https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=125261 (last visited Aug. 20, 2024).
[20] Amended Complaint at 1, CareFirst of M.D. v. Johnson & Johnson, Civil Action No. 2:23-cv-00629-JKW-LRL (E.D. Va. Feb. 5, 2024).
[21] Jonathan Gardner, *Acquired patents aid J&J defense of top-selling drug from biosimilar challenge*, BIOPHARMA DIVE (Mar. 29, 2023), https://www.biopharmadive.com/news/johnson-johnson-stelara-patents-amgen-biosimilar-momenta/646277/; Johnson & Johnson, 2021 Form 10-K at 3, https://www.sec.gov/ix?doc=/Archives/edgar/data/0000200406/000020040621000008/jnj-20210103.htm ("Janssen Biotech, Inc., a wholly-owned subsidiary of Johnson & Johnson, owns patents specifically related to STELARA®. The latest expiring United States patent expires in 2023"); Johnson & Johnson, 2022 Form 10-K at 3, https://www.sec.gov/ix?doc=/Archives/edgar/data/0000200406/000020040622000022/jnj-20220102.htm.
[22] Amended Complaint at 30-32, 51, CareFirst of M.D. v. Johnson & Johnson, Civil Action No. 2:23-cv-00629-JKW-LRL (E.D. Va. Feb. 5, 2024).
[23] *Id*. at 55-65.
[24] Press Release, Alvotech, STADA and Alvotech launch Uzpruvo, the first approved ustekinumab biosimilar to Stelara, across Europe (July 22, 2024), https://investors.alvotech.com/news-releases/news-release-details/stada-and-alvotech-launch-uzpruvo-first-approved-ustekinumab; Press Release, Amgen, Wezlana™ (Ustekinumab), A Biosimilar To Stelara®, Now Available In Canada For Certain Chronic Inflammatory Diseases (Mar. 4, 2024), https://www.amgen.ca/media/press-releases/2024/03/wezlana-ustekinumab-a-biosimilar-to-stelara-now-available-in-canada-for-certain-chronic-inflammatory-diseases.

Anticompetitive Uses of Biosimilar Manufacturing Patents

To understand Johnson & Johnson's anticompetitive use of manufacturing patents to deprive U.S. patients of more affordable biosimilars, simply look to Johnson & Johnson's own description of these patents in its litigation documents. In March 2023, Johnson & Johnson first asserted these patents in an infringement suit against Amgen, which had been seeking to market a biosimilar version of Stelara.[25] Johnson & Johnson acquired these patents from Momenta Pharmaceuticals, which Johnson & Johnson described as a "highly skilled biosimilar manufacturer [that] focused on manufacturing antibodies, including enabling biosimilars to more effectively match the reference product."[26]

Johnson & Johnson succinctly summarized the value of the patents it acquired from Momenta:

> Janssen's efforts have also included the acquisition of technologies developed by others in the antibody manufacturing industry. In particular, on October 1, 2020, Janssen acquired Momenta. Momenta's research and development included a substantial focus on methods of manufacturing biosimilar antibodies, including cell culturing processes that impact attributes of recombinant antibodies. **These patents are directed to enabling biosimilar manufacturers to use these processes to control attributes of the antibodies produced, thereby more precisely targeting the characteristics of the reference product**—and ultimately, producing a better copy than would otherwise be produced. Janssen now owns the '858, '889, '168, and '810 patent.[27] (emphasis added)

Johnson & Johnson repeatedly asserted that the value of these manufacturing patents lied in their ability to control attributes of antibodies and enable the manufacturing of biosimilars that targeted the characteristics of the reference biologic product. For example, the company stated, "Each of these Manufacturing Patents is directed to methods of using cell culturing processes to target and control features of biosimilar antibodies to assure equivalence to a reference product."[28] Later, Johnson & Johnson also stated, "The inventions covered by the Manufacturing Patents further and facilitate the production of biosimilar and interchangeable products by specifying methodologies to derive biosimilars that have the same chemical structure and clinical performance as the reference product."[29]

---

[25] First Amended Complaint, Janssen Biotech, Inc. v. Amgen, Inc., C.A. No. 22-1549-MN (D. Del. Mar. 7, 2023), https://www.bigmoleculewatch.com/wp-content/uploads/sites/2/2023/03/22-1549-Redacted-Complaint-AAA.pdf.
[26] *Id*. at ¶ 4.
[27] Id. at ¶ 26.
[28] *Id*. at ¶ 5.
[29] *Id*. at ¶ 6.

Stelara is not a biosimilar: it is the reference product. That is, these acquired manufacturing patents have nothing to do with producing Stelara, as evidenced by the fact that Johnson & Johnson did not even have ownership over these patents until 2020, eleven years after the approval of Stelara. Rather, these patents only have utility to biosimilar manufacturers, which wish to control features of their products and ensure equivalence with a branded biologic. It is difficult to articulate any pro-innovation effects or benefits to consumers by allowing branded manufacturers to acquire and assert biosimilar manufacturing patents solely for the purpose of blocking competitors from innovating their own more affordable options.

Thus, in Johnson & Johnson's own words, the company relies on patents acquired over a decade after Stelara's approval and specific to biosimilar manufacturing processes that have nothing to do with producing Stelara itself to thwart competition to its drug. This is perhaps one of the most blatant examples of anticompetitive patent practices on a drug selected for Medicare price negotiation. Because these patents expire in 2032 and 2033, Johnson & Johnson used them as leverage and extracted settlement terms that delay more affordable alternatives for patients in the United States until 2025, unlike other regions of the world where patients already have access to such lower-cost alternatives.

Method of Use Patent Claiming a Previously Disclosed Application

While Johnson & Johnson's patent in the active compound would have expired in September 2023, the company also asserted a patent covering Stelara's use for ulcerative colitis that expires in 2039 to increase its leverage in settlement negotiations with biosimilar manufacturers and delay biosimilar entry until 2025. Several manufacturers have argued before the Patent Trial and Appeal Board (PTAB) that Johnson & Johnson should not have been granted this patent because the claims for treating ulcerative colitis are obvious or anticipated over what was known at the time, including a publicly disclosed summary of the clinical trial the company was running for this indication.[30] More fundamentally, Johnson & Johnson's patent covering the active ingredient and set to expire in September 2023 already disclosed that the drug could be used to treat ulcerative colitis.[31] Johnson & Johnson thus obtained a secondary patent expiring **sixteen years** later by claiming a previously disclosed use of the drug.

As experts have written, pharmaceutical companies often file secondary patent applications that claim previously disclosed therapeutic applications of a drug in order to build out patent thickets that protect highly lucrative branded medicines from competition, prolong monopoly protections on medications, and consequently delay

[30] Petition for *Inter Partes* Review, Samsung Bioepis Co., Ltd. v. Janssen Biotech, Inc., IPR No. IPR2023-01103 (June 21, 2023), https://www.bigmoleculewatch.com/wp-content/uploads/sites/2/2023/06/PTAB-IR2023-01103-Petition.pdf; Petition for *Inter Partes* Review, Biocon Biologics, Inc. v. Janssen Biotech, Inc., IPR No. IPR2023-01444, https://www.bigmoleculewatch.com/wp-content/uploads/sites/2/2023/11/PTAB-IPR2023-01444-2.pdf (Nov. 22, 2023).

[31] *Compare* U.S. Pat. No. 6,902,734 col. 31 l. 30 *with* U.S. Pat. No. 10,961,307 Claim 1.

generic and biosimilar competition to the detriment of U.S. patients.[32] This appears to be precisely the kind of tactic Johnson & Johnson used to extend monopoly control on Stelara.

In sum, Johnson & Johnson engaged in patent abuses and evergreening practices that deprive patients of more affordable biosimilar alternatives until at least January 2025. First, the company exploited recently acquired patents that are specific to improving biosimilar manufacturing and have no obvious relevance to producing the original biologic, Stelara, in order to prevent and delay biosimilar competition. Second, the company obtained an evergreened patent that claimed an indication expiring sixteen years after a patent that previously disclosed that same therapeutic application.

Lastly, it is important to underscore that some manufacturers reached settlements to market biosimilars in 2025 through challenges to Johnson & Johnson's unfair patenting practices before the PTAB.[33] The PTAB is an administrative forum that provides a faster resolution mechanism for challenging problematic patents, like the ones used by Johnson & Johnson to extend Stelara's market exclusivity. But recent legislative proposals in the U.S. Senate, namely, the Promoting and Respecting Economically Vital American Innovation Leadership (PREVAIL) Act would make it harder to invalidate these obvious patents by, among other issues, raising the evidentiary standard in PTAB proceedings.[34] The predictable consequence of foreclosing PTAB as an effective forum for challenging pharmaceutical manufacturers' unfair patents is reduced leverage for obtaining settlements that expedite access to lower cost-alternatives. That would be devastating to U.S. patients.

Januvia (Sitagliptin)

Sitagliptin, marketed as Januvia by Merck, is a small molecule drug used to treat diabetes.[35] Medicare Part D spent more than $4 billion on the drug between June 2022 and May 2023.[36] The drug on average costs Medicare nearly $5,000 annually per enrollee, with

[32] I-MAK, ADDRESSING PATENT THICKETS TO IMPROVE COMPETITION AND LOWER PRESCRIPTION DRUG PRICE: A BLUEPRINT FOR REFORM 5 (2023).
[33]Press Release, Biocon, Biocon Biologics Secures US Market Entry Date for Bmab 1200, a Proposed Biosimilar to Stelara®, (Feb. 29, 2024), https://www.biocon.com/biocon-biologics-secures-us-market-entry-date-for-bmab-1200-a-proposed-biosimilar-to-stelara/; *Samsung Bioepis Secures US License Date for SB17, a Proposed Biosimilar to Stelara®*, BIOSPACE (Nov. 30, 2023), https://www.biospace.com/samsung-bioepis-secures-us-license-date-for-sb17-a-proposed-biosimilar-to-stelara.
[34] Promoting and Respecting Economically Vital American Innovation Leadership Act, S.2220 118th Congress (Introduced 7/10/2023).
[35] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).
[36] *Id*.

out-of-pocket costs amounting to more than $500 each year for enrollees who do not receive the low-income subsidy.[37] On this drug alone, Merck made $2.189 billion in 2023.[38]

Sitagliptin helps control blood sugar levels in people with type 2 diabetes by inhibiting an enzyme called dipeptidyl peptidase-IV, and the drug was approved by the FDA in 2006.[39] Januvia is a particular salt form of sitagliptin called a dihydrogenphosphate (DHP) salt of sitagliptin, which is made from reacting sitagliptin with phosphoric acid.[40] Patent protection for the drug in the United States is expected to expire in May 2027.[41] By comparison, Merck lost exclusivity for the drug in 2022 in Europe and China, and generics are already supplied, for example, in Australia and Canada.[42]

In the United States, Mylan sought FDA approval to manufacture a generic of Januvia, but Merck sued it for patent infringement in May 2019.[43] Mylan ultimately lost, but it appears that the company entered a settlement with Merck to sell a generic of Januvia earlier than the expiration dates of the patents-in-suit.[44] Merck has also entered settlements with 26 companies that sought to manufacture generics of Januvia, and a related product,

---

[37] *Id.*; ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES— MEDICARE ENROLLEES' USE AND OUT-OF-POCKET EXPENDITURES FOR DRUGS SELECTED FOR NEGOTIATION UNDER THE MEDICARE DRUG PRICE NEGOTIATION PROGRAM 5 (Aug. 29, 2023), https://aspe.hhs.gov/sites/default/files/documents/9a34d00483a47aee03703bfc565ffee9/ASPE-IRA-Drug-Negotiation-Fact-Sheet-9-13-2023.pdf .

[38] Merck, 2023 Form 10-K at 124, https://www.sec.gov/ix?doc=/Archives/edgar/data/310158/000162828024006850/mrk-20231231.htm.

[39] Merck Sharp & Dohme, LLC v. Mylan Pharm., No. 1:19CV101, at 4-5 (N.D. W.Va. Sep. 21, 2022), https://casetext.com/case/merck-sharp-dohme-llc-v-mylan-pharm; U.S. Food & Drug Admin., *Product Details for NDA 021995*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=021995#23642 (last visited Aug. 20, 2024).

[40] Merck Sharp & Dohme, LLC v. Mylan Pharm., No. 1:19CV101, at 7-11 (N.D. W.Va. Sep. 21, 2022).

[41] *Id*. at 12-13; U.S. Food & Drug Admin., *Patent and Exclusivity for: N021995*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=021995&Appl_type=N (last visited Aug. 20, 2024).

[42] Merck, 2023 Form 10-K at 53, https://www.sec.gov/ix?doc=/Archives/edgar/data/310158/000162828024006850/mrk-20231231.htm; *Sitagliptin*, PHARMACEUTICAL BENEFITS SCHEME, https://www.pbs.gov.au/medicine/item/11572C-11573D-11576G-13871C-14021Y-14058X-9180E-9181F-9182G (last visited Aug. 20, 2024); RÉGIE DE L'ASSURANCE MALADIE, LIST OF MEDICATIONS 488-89 (Aug. 14, 2024), https://www.ramq.gouv.qc.ca/sites/default/files/documents/non_indexes/liste-med-2024-08-14-en.pdf.

[43] Merck Sharp & Dohme, LLC v. Mylan Pharm., No. 1:19CV101, at 2-3 (N.D. W.Va. Sep. 21, 2022).

[44] Eric Sagonowsky, *Merck, Viatris close in on settlement in long-running Januvia patent case*, FIERCE PHARMA (Mar. 21, 2023), https://www.fiercepharma.com/pharma/merck-viatris-seek-stay-januvia-patent-case-finalize-settlement; Merck Sharp & Dohme, LLC v. Mylan Pharm, No . 23-1013 (Fed. Cir. 2023), https://cafc.uscourts.gov/opinions-orders/23-1013.ORDER.5-11-2023_2125391.pdf (dismissing Mylan's appeal of its district court loss in light of the parties' joint stipulation).

Janumet.[45] Merck states that the companies will be able to bring generics of Januvia and Janumet to market in May 2026, and potentially earlier.[46]

As others have highlighted, Merck is extending its monopolistic pricing power over Januvia through evergreening abuses, a drug which should have gone off patent in January 2023.[47] Merck claimed an obvious variation of sitagliptin based on its prior patent disclosures in order to prevent generic competition against its branded drug.

Patenting Previously Disclosed Forms and Uses of Sitagliptin

As stated above, Januvia is a specific salt form of sitagliptin created from reacting the compound with phosphoric acid.[48] Merck filed for a patent in 2002 directed to inhibitors of dipeptidyl peptidase-IV with a claim covering the sitagliptin compound, or "a pharmaceutically acceptable salt thereof" which was set to expire January 2023.[49] That patent also disclosed and claimed treating diabetes with compounds covered by the patent.[50] Importantly, the written description that precedes the patent claims disclosed that a salt can be formed by reacting non-toxic acids with basic compounds covered by the patent and **even lists phosphoric acid as one of eight preferred acids** for creating such salts.[51]

In 2004, Merck filed a patent with claims for the DHP salt of sitagliptin and a method for treating type 2 diabetes using a therapeutically effective amount of the salt, which is expected to expire May 2027.[52] The protection provided by the 2004 salt patent provides four additional years of monopoly control to Merck beyond the active compound patent that already disclosed creating a salt form from a reaction with a preferred acid, phosphoric acid. That is, the fact the earlier patent covering Januvia disclosed phosphoric acid as one of eight preferred acids to react with a basic compound, like sitagliptin, should have made the later patent's claim on the DHP salt of sitagliptin obvious and invalid.[53]

---

[45] Andrew Seidman, *How Merck extended its monopoly on a blockbuster diabetes drug*, PHILADELPHIA INQUIRER (Dec. 20, 2023), https://www.inquirer.com/business/merck-patent-januvia-medicare-price-negotiations-20231220.html.

[46] Merck, 2023 Form 10-K at 107, https://www.sec.gov/ix?doc=/Archives/edgar/data/310158/000162828024006850/mrk-20231231.htm.

[47] Andrew Seidman, *How Merck extended its monopoly on a blockbuster diabetes drug*, PHILADELPHIA INQUIRER (Dec. 20, 2023), https://www.inquirer.com/business/merck-patent-januvia-medicare-price-negotiations-20231220.html.

[48] Merck Sharp & Dohme, LLC v. Mylan Pharm., No. 1:19CV101, at 7-11 (N.D. W.Va. Sep. 21, 2022).

[49] *Id*. at 16-17; U.S. Pat. No. 6,699,871 Claim 17.

[50] U.S. Pat. No. US 6,699,871 Col. 9 l. 34-41, Claims 22 & 23.

[51] U.S. Pat. No. US 6,699,871 Col. 6 ll. 61-67, Col. 7 ll. 1-4.

[52] Merck Sharp & Dohme, LLC v. Mylan Pharm., No. 1:19CV101, at 11-13 (N.D. W.Va. Sep. 21, 2022); U.S. Food & Drug Admin., *Product Details for NDA 021995*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=021995#23642 (last visited Aug. 20, 2024).

[53] *Compare* U.S. Pat. No. US 6,699,871 Col. 6 ll. 61-67, Col. 7 ll. 1-4, Claim 17 *with* U.S. Pat. No. 7,326,708 Claims 1, 2 & 3.

Similarly, the earlier patent also disclosed using the compounds of the invention to treat Type 2 diabetes and claimed treating Type 2 diabetes in certain instances, which should have made the later claims for treating this indication with a more specific salt form of sitagliptin obvious and invalid.[54]

In sum, Merck's evergreening practices in the United States deprive Americans of more affordable generics that are already available in other countries. Merck unfairly extended its exclusivity over Januvia by patenting a particular salt form of the drug compound made from reacting it with phosphoric acid, when it had previously claimed salt forms of the compound generally and even disclosed phosphoric acid as one of eight preferred acids for the reaction. Similarly, Merck claimed treating indications with this particular salt form when those therapeutic applications had been previously disclosed and claimed in the earlier patent. Therefore, these patent claims on Januvia should never have been granted and the drug should have faced generic competition after January 2023.

Xarelto (Rivaroxaban)

Rivaroxaban, marketed as Xarelto from a collaboration between Johnson & Johnson and Bayer AG, is a small molecule drug for preventing and treating blood clots and reducing health risks for patients with coronary or peripheral heart disease.[55] Between June 2022 and May 2023, Medicare Part D spent over $6 billion covering the cost of Xarelto for its enrollees.[56] For Medicare enrollees who did not receive the low-income subsidy, the drug incurred over $600 in annual out-of-pocket costs just for this one drug.[57]

Johnson & Johnson received FDA approval for rivaroxaban in 2011.[58] The patent protection for two of three patents listed for Xarelto in the FDA's Orange Book[59] expire in

---

[54] *Compare* U.S. Pat. No. US 6,699,871 Col. 9 l. 34-41, Claims 22 & 23 *with* U.S. Pat. No. 7,326,708 Claim 19.

[55] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES: XARELTO: MEDICARE ENROLLEE USE AND SPENDING (Nov. 13, 2023), https://aspe.hhs.gov/reports/ira-research-series-medicare-drug-price-negotiation-program.

[56] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).

[57] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES— MEDICARE ENROLLEES' USE AND OUT-OF-POCKET EXPENDITURES FOR DRUGS SELECTED FOR NEGOTIATION UNDER THE MEDICARE DRUG PRICE NEGOTIATION PROGRAM 6 (Aug. 29, 2023), https://aspe.hhs.gov/sites/default/files/documents/9a34d00483a47aee03703bfc565ffee9/ASPE-IRA-Drug-Negotiation-Fact-Sheet-9-13-2023.pdf .

[58] U.S. Food & Drug Admin., *Product Details for NDA 022406*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=022406#23884 (last visited Aug. 20, 2024).

[59] The FDA's publication called the *Approved Drug Products with Therapeutic Equivalence Evaluations*, also known as the Orange Book, identifies small molecule drugs approved by the agency and these drugs' related patent and exclusivity information. *Approved Drug Products with Therapeutic Equivalence Evaluations | Orange Book*, U.S. FOOD & DRUG ADMIN., https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book (last visited Dec. 2, 2024).

February and May 2025.[60] But the protection for a third patent covering the 10 mg, 15 mg, and 20 mg tablets of the drug expires in 2034.[61] Protection for the last patent on the 2.5 mg tablet expires in 2039.[62] Bayer AG, in its annual report, describes that the patents covering the active ingredient of Xarelto in the U.S. expire in 2025.[63] Thus, the secondary patents in Xarelto prolong Johnson & Johnson's monopolistic pricing power over the drug and grant 23-28 years of exclusivity on the medicine after its approval.

Since May 2021, Johnson & Johnson and Bayer AG have been litigating against generic manufacturers to stave off competition against its blockbuster drug.[64] The lawsuits center patent infringement claims from the latest expiring patents in the Orange Book for the 2.5, 10, 15, and 20 mg tablets.[65] According to Bayer's annual reporting, the company entered a settlement with Unichem pharmaceuticals, which granted Unichem a license to sell generics of the 10, 15, and 20 mg tablets starting in 2027, or earlier under certain undisclosed circumstances.[66] Johnson & Johnson has additionally disclosed that it entered a confidential settlement with Biocon for alleged infringement of Xarelto's patents.[67] By comparison, other countries are already benefiting from generic supply of the medicine, such as Canada and France.[68]

Secondary Patent on the 2.5 mg Dosage of Rivaroxaban

The secondary patent on the 2.5 mg tablet of rivaroxaban is invalid because it claimed a method of treatment that was already known at the time the patent application was filed, as determined by the Patent Trial and Appeal Board. Three generic manufacturers filed petitions for *inter partes* review at the Patent Trademark Office seeking to invalidate claims from this patent (Patent No. 10,828,310, hereinafter "the '310 patent").[69] The Patent Trial

---

[60] U.S. Food & Drug Admin., *Product Details for NDA 022406*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=022406#23884 (last visited Aug. 20, 2024).
[61] *Id*.
[62] *Id*.
[63] Bayer, Bayer Annual Report 2023 at 49, https://www.bayer.com/sites/default/files/2024-03/bayer-annual-report-2023.pdf.
[64] Johnson & Johnson, 2023 Form 10-K at 97, https://www.sec.gov/ix?doc=/Archives/edgar/data/200406/000020040624000013/jnj-20231231.htm.
[65] *Id*. (stating that Patent Nos. 9,539,218 & 10,828,310 are at issue in the litigation, which are the latest expiring patents according to the Orange Book).
[66] Bayer, Bayer Annual Report 2023 at 50, https://www.bayer.com/sites/default/files/2024-03/bayer-annual-report-2023.pdf.
[67] Johnson & Johnson, 2023 Form 10-Q for the quarterly period ended October 1, 2023 at 35, https://www.sec.gov/ix?doc=/Archives/edgar/data/200406/000020040623000102/jnj-20231001.htm.
[68] RÉGIE DE L'ASSURANCE MALADIE, LIST OF MEDICATIONS 479-80 (Aug. 14, 2024), https://www.ramq.gouv.qc.ca/sites/default/files/documents/non_indexes/liste-med-2024-08-14-en.pdf; *RIVAROXABAN TEVA 10 mg, comprimé pelliculé*, BASE DE DONNÉES PUBLIQUE DES MÉDICAMENTS, https://base-donnees-publique.medicaments.gouv.fr/extrait.php?specid=64140958 (last visited Aug. 20, 2024).
[69] Mylan Pharmaceuticals Inc. v. Bayer Pharma Aktiengesellschaft, IPR2022-00517, at 2 (PTAB July 28, 2023), https://developer.uspto.gov/ptab-web/#/search/decisions (retrieved by searching Patent No. 10,828,310).

and Appeal Board (PTAB) found that the '310 patent was anticipated and obvious over what was known at the time and held the claims invalid on July 28, 2023.[70] Bayer, however, has appealed the decision to the Federal Circuit.[71]

The patent claims cover the combination therapy of rivaroxaban and aspirin to reduce the risk of heart attack, stroke, or death in patients with coronary or peripheral artery disease, and expires in 2039.[72] One set of claims covers the administration of 2.5 mg of rivaroxaban twice daily and 75-100 mg of aspirin once daily.[73] The other set of claims covers the once daily administration of a product containing 2.5 mg of rivaroxaban and 75-100 mg and a second product containing 2.5 mg of rivaroxaban.[74]

First, PTAB held that the claims covering the twice daily administration of 2.5 mg of rivaroxaban and 100 mg of aspirin were anticipated by a journal article published in 2016, before this patent was filed.[75] Anticipation, as explained by the PTAB, occurs if each and every element of the claim is found either expressly or inherently in a single prior art reference, i.e., a single source showing what was known prior to the patent's filing.[76] Even under the high legal threshold required for inherent anticipation, the PTAB found that the journal article inherently disclosed each element of the claim.[77] This is because the journal article discussed an ongoing clinical study of patients with coronary or peripheral artery disease in which some were given 2.5 mg of rivaroxaban twice daily and 100 mg of aspirin once daily.[78] This method of reducing the risk of heart attack, stroke, or death in these patients mirrored what the patent claims tried to subsequently cover, so PTAB held the claims invalid.[79]

---

[70] *Id*. at 27 & 37.

[71] Johnson & Johnson, 2023 Form 10-K at 97, https://www.sec.gov/ix?doc=/Archives/edgar/data/200406/000020040624000013/jnj-20231231.htm.

[72] U.S. Patent No. 10,828,310, Claims 1-8; U.S. Food & Drug Admin., *Product Details for NDA 022406*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=022406#23884 (last visited Aug. 20, 2024); Mylan Pharmaceuticals Inc. v. Bayer Pharma Aktiengesellschaft, IPR2022-00517, at 7-8 (PTAB July 28, 2023), https://developer.uspto.gov/ptab-web/#/search/decisions (retrieved by searching Patent No. 10,828,310).

[73] Mylan Pharmaceuticals Inc. v. Bayer Pharma Aktiengesellschaft, IPR2022-00517, at 7-8 (PTAB July 28, 2023), https://developer.uspto.gov/ptab-web/#/search/decisions (retrieved by searching Patent No. 10,828,310).

[74] *Id*.

[75] *Id*. at 22-27.

[76] *Id*. at 23.

[77] *Id*. at 24.

[78] *Id*. at 23-25.

[79] *Id*. at 24-27. Bayer argued in opposition that the previously disclosed ongoing clinical study did not satisfy the part of the claim stating "clinically effective proven" amounts of the drugs needed to be administered. According to Bayer's reasoning, the results of the study were not published yet, and the clinical results of the trial were not inherent to its method to result in anticipation of its patent claims. Even if the "clinically effective proven" amounts of the claim were material, which they were not since the claims already set out

In addition to finding that the patent claims were anticipated, the PTAB held the patent claims were obvious over this journal article's disclosed methods.[80] The PTAB also found the other claims regarding the coadministration of rivaroxaban with aspirin doses below 100 mg to be obvious because the claimed doses merely represented obvious variants of aspirin dosages that existed around the world. For example, in Germany aspirin also comes in 75 mg doses, and in the United States aspirin can come in 81 mg doses.[81] Further, another prior journal article disclosed a study co-administering rivaroxaban at 2.5 mg doses twice daily with these dose levels of aspirin, buttressing the PTAB's finding of obviousness.[82]

Given the fundamental promise of the patent system—that the public can freely access a patented invention upon the patent's expiration—it is flawed that the current system of intellectual property could allow monopoly protections on certain uses of a drug that would expire **nearly three decades** after a drug was initially approved. Further, the patent system should expand opportunities to challenge invalid patent claims that hurt U.S. patients. Instead, current legislative proposals, like the Promoting and Respecting Economically Vital American Innovation Leadership (PREVAIL) Act, would unduly constrain patent challenges at PTAB and harm patient access to lower cost-alternatives.[83]

Secondary Patents on the 10, 15, & 20 mg Dosage of Rivaroxaban

The 10, 15, & 20 mg doses of rivaroxaban were approved in 2011, with protection based on two patents set to expire in 2025.[84] Bayer had already received a patent term extension of 1356 days (almost four years) on one of these patents for time lost in the regulatory approval process.[85] But on top of that, U.S. Patent No. US 9,539,218 (the '218 patent) provides almost another decade of patent protection on these doses.[86] The earlier patents

---

the numerical dosages that are effective, PTAB applied Federal Circuit law that newly discovered results of known processes cannot be patented and that a prior art's disclosure can anticipate a claim where the disclosure, including teachings and methods, can show a natural result that would result in the claimed product. Here, the clinical study's results showing that the claimed administration is clinically effective is not patentable because the clinical study's method of administration indicated a natural result of clinical efficacy that was confirmed by the results of the study. *Id*. at 15-19, 25-27.

[80] *Id*. at 27-37.

[81] *Id*. at 33.

[82] *Id*. at 34.

[83] Promoting and Respecting Economically Vital American Innovation Leadership Act, S.2220 118th Congress (Introduced 7/10/2023).

[84] U.S. Food & Drug Admin., *Product Details for NDA 022406*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=022406#23884 (last visited Aug. 20, 2024).

[85] *Applications for patent term extension and patent terms extended under 35 U.S.C. § 156,* U.S. PAT. & TRADEMARK OFF., https://www.uspto.gov/patents/laws/patent-term-extension/patent-terms-extended-under-35-usc-156 (last visited Aug. 20, 2024).

[86] U.S. Food & Drug Admin., *Product Details for NDA 022406*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS,

cover the active ingredient, its combination with other substances to form the drug, the process of preparing the drug, a solid oral version of the drug, a rapid-release tablet, and the drug's use for preventing or treating thromboembolic diseases.[87] The primary marginal benefit claimed by the '218 patent is its protection **over a once-daily dose of the tablet variation** of the drug for at least five days to treat largely identical issues.[88] In contrast, Bayer itself states in its annual corporate statements that the patent covering 10, 15, and 20 mg once-daily tablet in Europe is set to expire in 2026.[89]

In sum, Bayer & Johnson and Johnson exploited two kinds of evergreening practices to extend monopoly control over Xarelto to the detriment of American patients. First, Bayer claimed an obvious method of treating cardiovascular indications using Xarelto and aspirin together that was known according to publicly available information to try and secure exclusivity on this method of treatment until 2039, twenty-eight years after the drug was initially approved. Second, Bayer claimed a daily dosing regimen of the drug to try and secure exclusivity until 2034, almost ten years after other patents were set to expire and twenty-three years after the drug's initial approval.

Eliquis (Apixaban)

Apixaban (marketed as Eliquis) is a blood thinner used to treat blood clots which received FDA approval in 2012, and is marketed through a collaboration between Bristol Myers Squibb (BMS) and Pfizer.[90] From June 2022 to May 2023, Medicare Part D spent a colossal $16,482,621,000 to cover the cost of Eliquis for more than 3.7 million enrollees.[91] The drug, on average, costs the program $4,448 per enrollee, with an annual out-of-pocket cost amounting to more than $600 for just this one drug among enrollees who did not receive low-income subsidies.[92] In 2023, BMS and Pfizer made a staggering $12.2 billion and $6.7

---

https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=022406#23884 (last visited Aug. 20, 2024).

[87] *See* U.S. Pat. Nos. 7,157,456 & 9,415,053.

[88] *Compare* U.S. Pat. No. 9,539,218 Claims 1-4 *with* U.S. Pat. Nos. 7,157,456 & 9,415,053.

[89] Bayer, Bayer Annual Report 2023 at 50, https://www.bayer.com/sites/default/files/2024-03/bayer-annual-report-2023.pdf.

[90] U.S. Food & Drug Admin., *Product Details for NDA 202155*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202155#30907 (last visited Aug. 20, 2024); Press Release, BMS, The Bristol-Myers Squibb-Pfizer Alliance is pleased with the U.S. District Court decision to uphold both the composition of matter (COM) patent (US 6,967,208) and formulation patent (US 9,326,945) covering Eliquis® (Aug. 5, 2020), https://news.bms.com/news/details/2020/The-Bristol-Myers-Squibb-Pfizer-Alliance-is-pleased-with-the-U.S.-District-Court-decision-to-uphold-both-the-composition-of-matter-COM-patent-US-6967208-and-formulation-patent-US-9326945-covering-Eliquis/default.aspx.

[91] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).

[92] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES— MEDICARE ENROLLEES' USE AND OUT-OF-POCKET EXPENDITURES FOR DRUGS SELECTED FOR NEGOTIATION UNDER THE MEDICARE DRUG PRICE NEGOTIATION PROGRAM 6 (Aug. 29, 2023),

billion off the drug, respectively.[93] Although the FDA approved generics for the drug in 2019,[94] none will come to market in the United States until April 1, 2028 because BMS and Pfizer had sued 25 generic manufacturers to delay generic competition on their lucrative drug.[95] By contrast, generics are already available in Canada and the United Kingdom.[96] To delay generic entry, BMS and Pfizer rely on a secondary patent covering a crystalline version of the active ingredient to unfairly extend monopoly control on the drug.

Prolonging Monopoly Protections with Crystalline Patents

According to the Orange Book, BMS's patent covering the drug substance for apixaban was filed in September 2002, and was set to expire in February 2023.[97] But BMS received an extension of its patent term until November 2026 from the U.S. Patent & Trademark Office using a federal law that can extend a patent term for time lost in the premarket government approval process.[98] BMS and Pfizer also own a patent on a crystalline version of apixaban that dissolves faster in the body, which increases its bioavailability (the amount of the drug that gets into the blood).[99] This patent extended exclusivity over the drug until 2031 and allowed the companies to extract settlement agreements delaying generic entry until 2028.[100]

---

https://aspe.hhs.gov/sites/default/files/documents/9a34d00483a47aee03703bfc565ffee9/ASPE-IRA-Drug-Negotiation-Fact-Sheet-9-13-2023.pdf .

[93] BMS, 2023 10-K Form at 45, https://www.sec.gov/ix?doc=/Archives/edgar/data/14272/000001427224000044/bmy-20231231.htm; Pfizer, 2023 10-K Form at 38, https://www.sec.gov/ix?doc=/Archives/edgar/data/78003/000007800324000039/pfe-20231231.htm.

[94] Press Release, U.S. Food & Drug Admin., FDA approves first generics of Eliquis (Jan. 10, 2020), https://www.fda.gov/news-events/press-announcements/fda-approves-first-generics-eliquis.

[95] BMS, 2023 10-K Form at 7, https://www.sec.gov/ix?doc=/Archives/edgar/data/14272/000001427224000044/bmy-20231231.htm; Bristol-Myers Squibb Co. v. Aurobindo Pharma U.S. Inc., 477 F. Supp. 3d 306, 311 n.1 (D. Del. 2020), https://casetext.com/case/bristol-myers-squibb-co-v-aurobindo-pharma-usa-inc-1.

[96] RÉGIE DE L'ASSURANCE MALADIE, LIST OF MEDICATIONS 393-94 (Aug. 14, 2024), https://www.ramq.gouv.qc.ca/sites/default/files/documents/non_indexes/liste-med-2024-08-14-en.pdf; David Wallace, *Teva Introduces First Eliquis Rival In UK,* GENERICS BULLETIN (May 31, 2022), https://generics.citeline.com/GB151923/Teva-Introduces-First-Eliquis-Rival-In-UK; WHITTINGTON HEALTH NHS TRUST, SWITCHING TO APIXABAN (GENERICS) (May 28, 2024).

[97] *Product Details for NDA 202155*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202155#30907 (last visited Aug. 20, 2024); U.S. Pat. No. 6,967,208.

[98] *Applications for patent term extension and patent terms extended under 35 U.S.C. § 156,* U.S. PAT. & TRADEMARK OFF., https://www.uspto.gov/patents/laws/patent-term-extension/patent-terms-extended-under-35-usc-156 (last visited Aug. 20, 2024).

[99] Bristol-Myers Squibb Co. v. Aurobindo Pharma U.S. Inc., 477 F. Supp. 3d 306, 355-56 (D. Del. 2020), https://casetext.com/case/bristol-myers-squibb-co-v-aurobindo-pharma-usa-inc-1.

[100] *Product Details for NDA 202155*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS,

As experts have written, crystalline patents are obvious variations of the original compound of a drug, the patenting of which allows drug companies to prolong their monopoly protections and block generic competitors.[101] This is because these variations can differ in important therapeutic properties, like drug product performance, bioavailability, and stability, so the FDA released guidance in 2000 recommending routine testing to monitor and control these forms as part of the approval process of drugs.[102] From the perspective of seeking to promote new and useful inventions, there is little value to awarding additional monopoly protections for a standard screening procedure employed widely by industry to monitor forms that already exist inherently in the original compound. These forms would be discovered in any case during the drug approval process.

In sum, BMS and Pfizer have leveraged this crystalline patent against manufacturers in settlements to unfairly delay generic entry until April 2028, when patent protection in the drug should have expired by November 2026. Medicare enrollees, as well as the public at large, will pay the hefty price for this evergreening practice given that the drug costs the program over $16 billion a year.

Imbruvica (Ibrutinib)

Ibrutinib (marketed as Imbruvica) is a small molecule drug used to treat blood cancers.[103] In 2015, AbbVie acquired Pharmacyclics, which co-developed the drug with Johnson & Johnson, for approximately $21 billion to obtain the drug Imbruvica, reflecting the profits AbbVie believed it could receive through monopoly pricing power over the drug.[104]

Between June 2022 and May 2023, Medicare Part D's gross expenditure for the drug was over $2.66 billion.[105] Of the 22,000 enrollees who used the drug, 18,000 did not receive the low-income subsidy.[106] Ibrutinib imposed the highest financial burden on these Medicare enrollees of all the drugs selected for negotiation, with an average out-of-pocket cost of

---

https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202155#30907 (last visited Aug. 20, 2024); U.S. Patent No. 9,326,945; BMS, 2023 10-K Form, at 45, https://www.sec.gov/ix?doc=/Archives/edgar/data/14272/000001427224000044/bmy-20231231.htm.

[101] I-MAK, ADDRESSING PATENT THICKETS TO IMPROVE COMPETITION AND LOWER PRESCRIPTION DRUG PRICE: A BLUEPRINT FOR REFORM 7 (2023).

[102] *Id*.

[103] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).

[104] Michael J. de la Merced & Andrew Pollack, *AbbVie to Pay $21 Billion for Pharmacyclics, Maker of a Promising Cancer Drug*, N.Y. TIMES (Mar. 4, 2015), https://www.nytimes.com/2015/03/05/business/dealbook/abbvie-to-pay-21-billion-for-pharmacyclics-maker-of-a-best-selling-cancer-treatment.html.

[105] *Id*.

[106] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES— MEDICARE ENROLLEES' USE AND OUT-OF-POCKET EXPENDITURES FOR DRUGS SELECTED FOR NEGOTIATION UNDER THE MEDICARE DRUG PRICE NEGOTIATION PROGRAM 5 (Aug. 29, 2023), https://aspe.hhs.gov/sites/default/files/documents/9a34d00483a47aee03703bfc565ffee9/ASPE-IRA-Drug-Negotiation-Fact-Sheet-9-13-2023.pdf .

$6,497 per enrollee per year.[107] While imposing significant financial challenges on American patients, AbbVie and Johnson & Johnson brought in approximately $3.596 billion and $3.264 billion, respectively, on the drug in 2023 alone.[108] Since the acquisition and through 2020, the drug has earned approximately $15 billion in net revenues.[109]

The U.S. House Committee on Oversight & Reform investigated AbbVie's pricing abuses on the drug, finding that the company raised the price of the drug from $99,776 at its launch in 2013 to $181,529 in 2021.[110] The investigation also found that Americans were charged double the price of the drug in other countries, including most high-income countries,[111] even though preclinical studies key to the drug's development relied on taxpayer funding.[112] The Committee found that, had Medicare been allowed to negotiate the price of Imbruvica and received the same discounts as the Departments of Defense and Veterans Affairs between 2014 and 2018, taxpayers would have saved $1.6 billion.[113] Significantly, the Committee found that AbbVie exploited the patent system to delay generic competition against Imbruvica.[114] Although nearly a dozen generic manufacturers sought FDA approval of generics, most entered confidential agreements with the company to delay generic entry until at least 2032, which is six years after the original patents were expected to expire.[115]

Drip-Feed Patenting

According to the Committee, the company amassed a massive patent thicket to deter any generic manufacturer from bringing a more affordable alternative to market. Relying on findings from the Initiative for Medicines, Access, and Knowledge (I-MAK), the Committee reported that, although Pharmacyclics (later acquired by AbbVie) filed the initial patents in ibrutinib's active ingredient in 2006 and expected to expire in 2026, over 150 patent applications had been filed on the drug to try and bar generic competition until

---

[107] *Id*. at 6.
[108] AbbVie Inc., 2023 Form 10-K at 93, https://www.sec.gov/ix?doc=/Archives/edgar/data/1551152/000155115224000011/abbv-20231231.htm; Johnson & Johnson, 2023 Form 10-K at 83, https://www.sec.gov/ix?doc=/Archives/edgar/data/200406/000020040624000013/jnj-20231231.htm.
[109] U.S. H.R. COMM. OVERSIGHT & REFORM, STAFF REP. DRUG PRICING INVESTIGATION: ABBVIE—HUMIRA & IMBRUVICA 5 (May 2021).
[110] *Id*. at 3.
[111] *Id*. at 12.
[112] ARIANNA SCHOUTEN, KNOWLEDGE ECOLOGY INTERNATIONAL, NOTES ON THE PRECLINICAL DEVELOPMENT OF IMBRUVICA (IBRUTINIB) (Oct. 2, 2023), https://www.keionline.org/wp-content/uploads/KEI-BN-2023-4.pdf.
[113] U.S. H.R. COMM. OVERSIGHT & REFORM, STAFF REP. DRUG PRICING INVESTIGATION: ABBVIE—HUMIRA & IMBRUVICA 15 (May 2021).
[114] *Id*. at 36.
[115] *Id*. at 37. AbbVie Inc., 2023 Form 10-K at 7, https://www.sec.gov/ix?doc=/Archives/edgar/data/1551152/000155115224000011/abbv-20231231.htm.

2036.[116] Eighty-eight patents had been granted for the drug.[117] Over half of these patent applications were filed after the drug's FDA approval in 2013, showing that they were not necessary for the research and development of the drug.[118]

The Committee detailed how AbbVie used a "drip-feed" patent strategy to prolong monopoly power over ibrutinib.[119] "Under this strategy, AbbVie filed multiple additional patents covering aspects of Imbruvica that had already been disclosed in earlier patents but with more specificity."[120] For example, the Committee reported Pharmacyclics first disclosed (but did not claim) that Imbruvica could be used to treat chronic lymphocytic leukemia (CLL) and Waldenstrom macroglobulinemia (WM) in a patent application from 2006 covering the drug's active ingredient.[121] Later, Pharmacyclics filed patent applications covering the dosing of Imbruvica to treat these two conditions in 2013 and 2014, extending patent protection by five years into 2031.[122] And in 2016, after Pharmacyclics was acquired by AbbVie, the company filed for another patent covering a solid tablet formulation of the drug, extending patent protection on the drug until 2036.[123] AbbVie has leveraged patent protection intended to grant three decades of exclusivity on the drug, and potentially 23 years of monopoly pricing power on the drug since its approval in 2013, to extract settlement agreements delaying generic entry until 2032.[124] These evergreening abuses harm American patients, including Medicare enrollees.

Additionally, it is worth noting that, like with Eliquis, AbbVie also uses a crystalline patent that is set to expire in December 2033 to extend exclusivity, seven years after the expiry of the primary patents in the compound.[125] As stated previously, crystalline variations of drug compounds are regularly screened for during the drug approval process because they can differ in important therapeutic properties, and it is flawed to grant patent protection for these obvious variants that would have been discovered in any case.[126] For example, a generic company argued in patent litigation that the crystalline patent claims were obvious because a person of ordinary skill would have been motivated

---

[116] U.S. H.R. COMM. OVERSIGHT & REFORM, STAFF REP. DRUG PRICING INVESTIGATION: ABBVIE—HUMIRA & IMBRUVICA 36 (May 2021).
[117] I-MAK, OVERPATENTED, OVERPRICED: IMBRUVICA'S PATENT WALL 2 (July 2020).
[118] U.S. H.R. COMM. OVERSIGHT & REFORM, STAFF REP. DRUG PRICING INVESTIGATION: ABBVIE—HUMIRA & IMBRUVICA 37 (May 2021).
[119] *Id*. at 36.
[120] *Id*.
[121] *Id*.
[122] *Id*.
[123] *Id*.
[124] *Id*. at 37; AbbVie Inc., 2023 Form 10-K at 7, https://www.sec.gov/ix?doc=/Archives/edgar/data/1551152/000155115224000011/abbv-20231231.htm.
[125] U.S. Pat. No. 9,296,753; *Patent and Exclusivity for: N210563,* ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=210563&Appl_type=N (last visited Aug. 21, 2024).
[126] I-MAK, ADDRESSING PATENT THICKETS TO IMPROVE COMPETITION AND LOWER PRESCRIPTION DRUG PRICE: A BLUEPRINT FOR REFORM 7 (2023).

to develop the most stable version of ibrutinib, which was the specific crystalline form claimed in the patent, and would have had a reasonable expectation of doing so.[127] The Federal Circuit rejected this claim, deferring to factual findings of the district court that credited opposing testimony and found that discovering new crystalline forms "is challenging and unpredictable."[128]

Most recently, AbbVie sued a competitor (not a generic) to Imbruvica for infringing a patent that was issued in July 2023 (nearly ten years after Imbruvica's initial approval), demonstrating the continuous danger of evergreening practices. The National Comprehensive Cancer Network found the rival to be superior to Imbruvica in several areas due to the latter's toxicity, but AbbVie sued for damages against the competitor, alleging that the competitor's product violated its recently issued patent on treating chronic lymphocytic leukemia or small lymphocytic lymphoma using certain chemical compounds.[129] Notably, according to the Orange Book, Pharmacyclics had already listed patents granted more than a decade ago covering Imbruvica's use for treating chronic lymphocytic leukemia and small lymphocytic lymphoma.[130]

In sum, the evergreening practices on Imbruvica show how pharmaceutical companies can obtain multiple additional patents covering aspects of a drug that had already been disclosed in earlier patents but with more specificity and how companies use crystalline patents to extend monopoly control on drugs. More recently, AbbVie continues to guard its highly lucrative drug using patents with questionable innovative value.

Jardiance (Empagliflozin)

Empagliflozin, marketed as Jardiance by Boehringer Ingelheim and Eli Lilly, is a small molecule drug for treating diabetes and heart failure.[131] Twenty-eight percent (28%) of Medicare enrollees have diabetes, whereas 15% have been diagnosed with heart failure.[132] Between June 2022 and May 2023, Medicare Part D spent over $7 billion covering the cost

[127] Pharmacyclics, LLC v. Alvogen, Inc., Case No. 21-2270, at 22-23 (Fed. Cir. 2022), https://cafc.uscourts.gov/opinions-orders/21-2270.OPINION.11-15-2022_2033497.pdf.
[128] *Id*.
[129] Angus Liu, *AbbVie sues BeiGene over brand-new Imbruvica patent as blood cancer rivalry heats up*, FIERCE PHARMA (June 14, 2023), https://www.fiercepharma.com/pharma/abbvie-sues-beigene-over-brand-new-imbruvica-patent-blood-cancer-battle-heats; Complaint, Pharmacyclics LLC v. BeiGene USA, Inc., Case No. 1:23-cv-00646-UNA (D. Del. June 13, 2023), https://insight.rpxcorp.com/litigation_documents/15254746.
[130] U.S. Food & Drug Admin., *Patent and Exclusivity for: N210563,* ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=210563&Appl_type=N (last visited Aug. 21, 2024); U.S. Pat. Nos. 8,497,277 & 8,476,284.
[131] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES: JARDIANCE: MEDICARE ENROLLEE USE AND SPENDING (Nov. 8, 2023), https://aspe.hhs.gov/reports/ira-research-series-medicare-drug-price-negotiation-program
[132] *Id*.

of this prescription for its enrollees.[133] It was the second highest spend for Medicare Part D in terms of gross expenditures.[134] For enrollees who did not receive the low-income subsidy, the drug incurred almost $500 in annual out-of-pocket costs.[135]

The FDA approved empagliflozin for helping control blood glucose levels in people with type 2 diabetes in 2014.[136] But according to the FDA's Orange Book, the patent protection provided by 10 patents and 8 patents for the 10 mg and 25 mg doses of the drug, respectively, may expire as late as 2034 which is almost 20 years after the drug's initial approval.[137] According to Eli Lilly's filings with the Securities and Exchange Commission, Boehringer Ingelheim sued manufacturers seeking to bring generics of Jardiance to market in 2018 and lawsuits were pending as of September 2023.[138] At least some of these cases have resulted in settlements with terms stating that Boehringer Ingelheim's patents are valid and preventing two manufacturers from producing generics through the expiration of the patents.[139]

Patents on Previously Disclosed Elements, Crystalline Forms, & Checking Efficacy

Like the other pharmaceutical companies manufacturing drugs selected for Medicare price negotiation, Boehringer Ingelheim has engaged in evergreening abuses to manipulate its exclusivity over Jardiance. The patent protection for the drug compound, derived from the patent listed in the Orange Book, would have expired in 2025.[140] But Boehringer Ingelheim received a patent term extension of 1000 days (nearly 3 years) for time lost in the regulatory approval process, and received a pediatric exclusivity extension

---

[133] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).
[134] *Id*.
[135] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES— MEDICARE ENROLLEES' USE AND OUT-OF-POCKET EXPENDITURES FOR DRUGS SELECTED FOR NEGOTIATION UNDER THE MEDICARE DRUG PRICE NEGOTIATION PROGRAM 6 (Aug. 29, 2023), https://aspe.hhs.gov/sites/default/files/documents/9a34d00483a47aee03703bfc565ffee9/ASPE-IRA-Drug-Negotiation-Fact-Sheet-9-13-2023.pdf .
[136] U.S. Food & Drug Admin., *Product Details for NDA 204629*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=204629#32050 (last visited Aug. 22, 2024).
[137] *Id*.
[138] Eli Lilly & Co., Form 10-Q for the quarterly period ended Sept. 30, 2023 at 29, https://www.sec.gov/ix?doc=/Archives/edgar/data/0000059478/000005947823000284/lly-20230930.htm.
[139] *ANDA Litigation Settlements: Reported Settlements in Federal District Court Cases*, ROBINS & KAPLAN LLP, https://www.robinskaplan.com/resources/legal-updates/generically-speaking-hatch-waxman-bulletin/2021/generically-speaking-summer-2021/anda-litigation-settlements (last visited Aug. 22, 2024).
[140] *Applications for patent term extension and patent terms extended under 35 U.S.C. § 156*, U.S. PAT. & TRADEMARK OFF., https://www.uspto.gov/patents/laws/patent-term-extension/patent-terms-extended-under-35-usc-156 (last visited Aug. 20, 2024).

until 2029.[141] This patent already disclosed the drug compound could be used with other drugs, like metformin and the class of drugs to which linagliptin belongs.[142] Boehringer Ingelheim later claimed Jardiance's use with these drugs in patents expiring in 2030 and 2034, sometimes in narrower treatment contexts.[143] Boehringer also patented crystalline forms of the drug that expanded its protection expiring in 2027,[144] which as discussed above, should be invalid because of the need to screen for these forms during the drug approval process.

But most concerning is the secondary patents on the use of empagliflozin with patients suffering from renal impairment. The FDA recommends that patients' renal function be assessed before starting empagliflozin due to safety and efficacy concerns,[145] but Boehringer claimed the method of assessing patients' renal function before starting empagliflozin in patents expiring in 2034.[146] Thus, Boehringer Ingelheim may exploit these patents to exclude generics until 2034 despite the expiry of its drug compound patent in 2029. It is particularly problematic that Boehringer Ingelheim may artificially prolong its monopoly on empagliflozin by five years simply by patenting methods to ensure the safety and efficacy of the drug in patients. Boehringer Ingelheim's patent on screening patients for use of empagliflozin is like the problematic practice increasing among biologics in which manufacturers patent methods of diagnosis necessary for identifying patients eligible for, or most likely to respond, to a treatment.[147]

In sum, Boehringer Ingelheim has engaged in evergreening abuses to unfairly extend and expand monopoly protections over Jardiance. The evergreening practices include patenting the coadministration of the Jardiance with other drugs, the combination of which the company had already disclosed in earlier patents; patenting crystalline versions of the drug that should be obvious; and patenting methods for checking the drug's safety

---

[141] *Id*.; U.S. Food & Drug Admin., *Product Details for NDA 204629*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=204629#32050 (last visited Aug. 22, 2024).

[142] U.S. Pat. No. 7,579,449, Col. 30 ll. 49 – 67.

[143] U.S. Pat. No. 10,258,637, Claims 6, 12, 18, & 24; U.S. Pat. No. 11,090,323, Claims 6, 12, 18, & 24; U.S. Pat. No. 8,551,957.

[144] U.S. Pat. No. 7,713,938.

[145] *New Drug Application (NDA): 204629,* U.S. FOOD & DRUG ADMIN., https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/204629s040lbl.pdf (last visited Aug. 22, 2024) (discussing assessing renal function under "dosing and administration" and related safety and efficacy reasons in Section 8.6 of Jardiance's label).

[146] U.S. Pat. No. 11,090,323, Claims 7, 19, 30, & 40; U.S. Pat. No. 10,258,637, Claims 7, 19; U.S. Pat. No. 9,949,998, Claims 4, 10; U.S. Pat. No. 11,833,166, Claims 1, 7, 13, & 19; U.S. Food & Drug Admin., *Product Details for NDA 204629*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=204629#32050 (last visited Aug. 22, 2024).

[147] I-MAK, Overpatented, Overpriced: Keytruda's Patent Wall 3-4, 5 (May 2021), https://www.i-mak.org/wp-content/uploads/2021/05/i-mak.keytruda.report-2021-05-06F.pdf.

and efficacy in patients to extend exclusive control beyond the expiry of its drug compound patent.

Farxiga (Dapagliflozin)

Dapagliflozin, marketed as Farxiga by AstraZeneca, is a small molecule drug for treating diabetes, heart failure, and chronic kidney disease.[148] Between June 2022 and May 2023, Medicare Part D spent over $3 billion covering the cost of this prescription for its enrollees.[149] For enrollees who did not receive the low-income subsidy, the drug costs almost $450 a year in out-of-pocket costs.[150]

The FDA first approved Farxiga in 2014.[151] Whereas AstraZeneca's patents will forestall generic competition in the United States for the foreseeable future, other countries, like Canada, have already obtained generic competitors for their residents.[152] Like the other drugs subject to Medicare price negotiation, Farxiga has multiple layers of patent protection, some of which are unjustified.

Secondary Patents on Dapagliflozin

AstraZeneca has built a wall of secondary practices to try and insulate its drug from generic competition. According to the Orange Book, there are two patents covering the drug substance, or its active ingredient.[153] The first patent covering the drug substance (the active ingredient) is set to expire in 2026.[154] It was originally supposed to expire in 2020, but a patent term extension of 5 years was granted for time lost in the regulatory approval

---

[148] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES: FARXIGA: MEDICARE ENROLLEE USE AND SPENDING (Nov. 2, 2023), https://aspe.hhs.gov/reports/ira-research-series-medicare-drug-price-negotiation-program.

[149] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).

[150] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES— MEDICARE ENROLLEES' USE AND OUT-OF-POCKET EXPENDITURES FOR DRUGS SELECTED FOR NEGOTIATION UNDER THE MEDICARE DRUG PRICE NEGOTIATION PROGRAM 6 (Aug. 29, 2023), https://aspe.hhs.gov/sites/default/files/documents/9a34d00483a47aee03703bfc565ffee9/ASPE-IRA-Drug-Negotiation-Fact-Sheet-9-13-2023.pdf.

[151] U.S. Food & Drug Admin., *Product Details for NDA 202293*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202293#31420 (last visited Aug. 22, 2024).

[152] RÉGIE DE L'ASSURANCE MALADIE, LIST OF MEDICATIONS 416-17 (Aug. 14, 2024), https://www.ramq.gouv.qc.ca/sites/default/files/documents/non_indexes/liste-med-2024-08-14-en.pdf.

[153] U.S. Food & Drug Admin., *Product Details for NDA 202293*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202293#31420 (last visited Aug. 22, 2024).

[154] U.S. Pat. No. 6,515,117; U.S. Food & Drug Admin., *Product Details for NDA 202293*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202293#31420 (last visited Aug. 22, 2024).

process; it also received pediatric exclusivity protections.[155] However, a second patent covering crystalline forms of the drug compound extends exclusivity until 2030, more than four years after the other patent on the active ingredient is set to expire.[156]

Besides these two drug substance patents, there are 13 other patents covering the 5 mg dose of the drug and 16 other patents protecting the 10 mg dose of dapagliflozin.[157] For the 5 mg and 10 mg dose, there are five drug product patents. One of these appears to have been incorrectly listed in the Orange Book because it does not cover the drug, and accordingly has been requested to be delisted.[158] The other four drug product patents claim combining the active ingredient with other substances to create forms of delivery (a capsule, tablet, or granule), an immediate release formulation, compositions made with a crystalline version of the drug compound, the dosing regimen, and the drug products' use for treating diabetes.[159] These patents provide another layer of protection on Farxiga, as their patent protection expires between June 2027 and August 2028.

Finally, there are eight method of treatment patents that provide an additional layer of protection on Farxiga. These patents are particularly problematic since the drug substance patent expiring in 2025 already claimed a variety of therapeutic applications, including "treating or delaying progression or onset of diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension, or for increasing high density lipoprotein levels."[160] The additional method of treatment patent claims cover only the use of an entirely different antidiabetic medication and make no mention of dapagliflozin, some of which were rejected for obviousness-type double patenting;[161] using the drug product (the drug compound and other substances in the form of a capsule, tablet, or granule) to treat a list

---

[155] *Applications for patent term extension and patent terms extended under 35 U.S.C. § 156,* U.S. PAT. & TRADEMARK OFF., https://www.uspto.gov/patents/laws/patent-term-extension/patent-terms-extended-under-35-usc-156 (last visited Aug. 20, 2024).

[156] U.S. Pat. No. 7,919,598.

[157] U.S. Food & Drug Admin., *Product Details for NDA 202293*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202293#31420 (last visited Aug. 22, 2024).

[158] U.S Pat. No. 8,721,615.

[159] U.S. Pat. No. 7,851,502; U.S. Pat. No. 8,221,786; U.S. Pat. No. 8,501,698; U.S. Pat. No. 8,716,251.

[160] US Pat. No. No. 6,515,117, Claim 14; Col. 13, ll. 43-65, Col. 14, ll. 57-65; Col. 15, ll. 64-67.

[161] U.S. Pat. No. 7,456,254; U.S. Pat. No. 8,329,648; U.S. Pat. No. 8,906,851; U.S. Pat. No. 9,238,076; U.S. Pat. No. 8,431,685; U.S. Food & Drug Admin., *Product Details for NDA 202293*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202293#31420 (last visited Aug. 22, 2024). PTO issued Non-Final Rejections for the patent applications that issued as U.S. Pat. Nos. 8,906,851; 9,238,076; and 8,431,685, in part, due to obviousness-type double patenting. *Patent Center*, U.S. PAT. & TRADEMARK OFF., https://patentcenter.uspto.gov/ (retrieved by searching patent numbers).

of identical indications to the abovementioned, previously claimed conditions, and other conditions known to be related to diabetes (like glucose tolerance);[162] and treating extreme insulin resistance and/or providing glycemic control after certain other drugs have failed, which has clear overlap with prior claims on treating insulin resistance.[163] The protection for these patents expires between 2024 and 2030.[164] The 10 mg tablet version of Farxiga has 3 additional method of treatment patents for using the drug to reduce certain cardiovascular risks in patients without diabetes, which expire in 2040.[165]

The spread of patents AstraZeneca has on dapagliflozin demonstrates an intent to prolong exclusive control over the drug. Like other companies, AstraZeneca incrementally patented the drug compound; the drug product; crystalline versions of the drug; and various methods of use, many of which had been claimed or were obvious over methods of use claimed in prior patents. For some of the more recent indications of the drug related to heart failure, the patent protection expires almost 14 years after the patent covering the drug substance expires and 26 years after the drug's initial approval. Even if these indications deserve extended exclusivity, there are serious questions as to whether protection should extend so long after the drug's initial approval and expiration of the protection in the drug compound.

Entresto (Sacubitril/Valsartan)

Sacubitril/valsartan, marketed by Novartis in the U.S. as Entresto, is a small molecule fixed-dose combination drug used to treat heart failure.[166] The FDA first approved Entresto in 2015, followed by approval for an expanded indication in 2021 for treating a subset of patients with a type of heart failure, called heart failure (HF) with preserved ejection fraction (HFpEF) for which no treatments had been available.[167] In 2024, the FDA approved a new dosage form, Entresto Sprinkle (oral pellets), which can be substituted

[162] U.S. Pat. No. 8,361,972.
[163] U.S. Pat. No. 8,685,934.
[164] U.S. Food & Drug Admin., *Product Details for NDA 202293*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=202293#31420 (last visited Aug. 22, 2024).
[165] U.S. Pat. No. 10,973,836; U.S. Pat. No. 11,826,376; U.S. Pat. No. 11,903,955.
[166] *New Drug Application (NDA): 207620*, U.S. FOOD & DRUG ADMIN., https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=207620 (last visited Aug. 23, 2024); ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES: ENTRESTO: MEDICARE ENROLLEE USE AND SPENDING (Nov. 1, 2023), https://aspe.hhs.gov/sites/default/files/documents/5bc9a571d6ece32ed3afae52f490d66b/Entresto.pdf.
[167] Press Release, Novartis, Novartis Entresto® granted expanded indication in chronic heart failure by FDA (Feb. 16, 2021), https://www.novartis.com/news/media-releases/novartis-entresto-granted-expanded-indication-chronic-heart-failure-fda-0; ; Letter from Patrizia Cavazzoni, Dir., Ctr. Drug Eval. & Res., U.S. Food & Drug Admin., to David Platt, VP & Medical Head, Cardiovascular & Metabolism, U.S. Clinical Dev. & Medical Affs., Novartis Pharmaceuticals Corp., at 32 (July 24, 2024), https://www.regulations.gov/document/FDA-2022-P-2228-0015.

for patients unable to swallow the prior tablet version.[168] From June 2022 to May 2023, gross expenditure for Entresto under Medicare Part D was $2,884,877,000.[169] Of the 521,000 enrollees who used the drug, 318,000 did not receive the low-income subsidy, and those patients incurred an out-of-pocket cost of over $500 per year.[170] Yet, in the 2023 financial year, Novartis earned $6.035 billion from sales of Entresto, of which $3.067 billion was in the U.S. alone.[171]

In May and July 2024, the FDA approved generic versions of sacubitril/valsartan from several applicants for all three dosage strengths for which Entresto is registered.[172] The FDA approvals mean that generic manufacturers can launch their products at-risk while patent litigation continues to unfold in the U.S. Novartis has also reportedly entered confidential settlements with other generic manufacturers to date.[173] In its more recent bids to keep generics of Entresto off the market, Novartis sued the FDA for granting generic approvals of the drug and, separately, lost its motion for a preliminary injunction to prevent MSN's at-risk launch of its generic in August 2024.[174]

Extending Monopoly Control through Multiple Patents on Drug Combinations, Crystalline Patents, & Method of Use Patents

Novartis has engaged in similar evergreening tactics as the other manufacturers of drugs selected for Medicare price negotiation. In a patent that expired in May 2024, Novartis had claimed the pharmaceutical composition combining sacubitril and valsartan to

---

[168] *New Drug Application (NDA): 207620*, U.S. FOOD & DRUG ADMIN., https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/218591Orig1s000,207620Orig1s025lbl.pdf (discussing that Entresto Sprinkle can be substituted in patients unable to swallow tablets at Section 2.5 of the FDA approved label).

[169] The White House, *FACT SHEET: Biden-Harris Administration Announces First Ten Drugs Selected for Medicare Price Negotiation*, STATEMENTS & RELEASES (Aug. 29, 2023).

[170] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES— MEDICARE ENROLLEES' USE AND OUT-OF-POCKET EXPENDITURES FOR DRUGS SELECTED FOR NEGOTIATION UNDER THE MEDICARE DRUG PRICE NEGOTIATION PROGRAM 6 (Aug. 29, 2023), https://aspe.hhs.gov/sites/default/files/documents/9a34d00483a47aee03703bfc565ffee9/ASPE-IRA-Drug-Negotiation-Fact-Sheet-9-13-2023.pdf.

[171] Novartis, 2023 Annual Report at F-19, https://www.sec.gov/Archives/edgar/data/1114448/000137036824000008/a240131-99_1.pdf.

[172] *New Drug Application (NDA): 207620*, U.S. FOOD & DRUG ADMIN., https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=207620 (last visited Aug. 23, 2024).

[173] Kevin Dunleavy, *After series of patent lawsuits, Novartis doubles down in Entresto defense with FDA complaint*, FIERCE PHARMA (Aug. 1, 2024), https://www.fiercepharma.com/pharma/novartis-sues-fda-over-approval-generic-version-its-bell-cow-entresto.

[174] Frasier Kansteiner, *Novartis loses bid to thwart launch of MSN's Entresto generic—for now*, FIERCE PHARMA (Aug. 13, 2024), https://www.fiercepharma.com/pharma/novartis-loses-bid-thwart-launch-msns-entresto-generic-now.

achieve a greater anti-hypertensive effect than their sum alone.[175] Another patent expiring in July 2025 covers the drug product comprising the two drug compounds and a carrier, where they are administered in combination in an approximate ratio of 1:1, where the amounts are effective to treat hypertension and heart failure, and its administration form of a tablet or capsule.[176]

Two patents additionally expire in 2027. One expires in May 2027 and covers a method of treating hypertension and heart failure using a "compound comprising non-covalently bound valsartan and sacubitril salts."[177] Another patent expires in November 2027 and claims crystalline forms of this non-covalently bound compound.[178]

Novartis has four patents that expire between 2033 and 2036, all of which claim methods of treatment. The company has three patents claiming methods of treatment for a subset of patients suffering from heart failure with preserved ejection fraction which expire in August 2033.[179] Finally, a patent expiring in May 2036 covers dosing regimens for treating chronic heart failure using sacubitril-valsartan by titrating up from half the recommended starting dose in patients not on other certain drugs, or low doses of these drugs.[180] Entresto sprinkle, which is the pellet version of the drug, is covered by many of the same (but not

[175] U.S. Pat. No. 7,468,390; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

[176] U.S. Pat. No. 8,101,659; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

[177] U.S. Pat. No. 9,388,134 (some of these claims are also specific to using the crystalline version of the compound for these methods of treatment); In re Entresto (Sacubitril/Valsartan) Patent Litigation, No. 20-md-2930-LPS, at 5 (D. Del. Jul. 8, 2021), https://casetext.com/case/in-re-entresto-sacubitrilvalsartan-patent-litig#N196698; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

[178] U.S. Pat. No. 8,877,938; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

[179] U.S. Pat. No. 9,517,226; U.S. Pat. No. 9,937,143; U.S. Pat. No. 11,135,192; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

[180] U.S. Pat. No. 11,058,667; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

all) patents.[181] However, it has one additional patent expiring in February 2037 covering the minitablet form and methods of using these minitablets for (1) treating heart failure in pediatric patients and (2) treating chronic heart failure and various other conditions in patients who require low or individual dosing or have difficulty swallowing.[182]

Novartis's pattern of patenting on Entresto demonstrates an intent to extend exclusivity over the drug. First, Novartis had earlier patents covering the combination of valsartan and sacubitril which expired in 2024 and 2025, but also later-expiring patents in 2027 covering the specific bonded complex of the two drugs that make up Entresto. Last year, a Court ruled that one of the earlier patents could not have claimed the complex that makes up Entresto because they did not exist at the time of the patent's priority date.[183] That is, the Court determined that Novartis had tried to claim an invention in an earlier patent that the inventor did not actually possess at the time of the priority date (the filing date of a patent application that the applicant relies on).[184] Building on its duplicative protection, Novartis, like other manufacturers of the drugs subject to price negotiation, separately patented crystalline forms of the specific complex to extend exclusivity until November 2027, which should be considered obvious.[185]

Finally, generics had circumvented Novartis's method of use patents expiring in 2033 and 2036 by adopting a skinny label, where they carved out the patented methods of treatment from their labels, but Novartis petitioned against, and now has sued, the FDA for granting the generic applications on this basis.[186] Novartis argues that it is impermissible to allow these carveouts in the labels, including for safety and efficacy reasons, and effectively attempts to extend monopoly control over Entresto using method of use patents expiring approximately 9-12 years after the other patents listed in the Orange Book and 21 years

---

[181] U.S. Pat. 10,722,471; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

[182] U.S. Pat. 10,722,471; U.S. Food & Drug Admin., *Patent and Exclusivity for: N207620*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=207620&Appl_type=N (last visited Aug. 23, 2024).

[183] In re Entresto Sacubitril/Valsartan Patent Litig., MDL 20-2930-RGA, at 42-45 (D. Del. Jul. 7, 2023), https://casetext.com/case/in-re-entresto-sacubitrilvalsartan-patent-litig-2.

[184] *Id*.

[185] U.S. Pat. No. 8,877,938, Col. 16, ll. 59-64, Claim 1; I-MAK, ADDRESSING PATENT THICKETS TO IMPROVE COMPETITION AND LOWER PRESCRIPTION DRUG PRICE: A BLUEPRINT FOR REFORM 7 (2023).

[186] Kevin Dunleavy, *After series of patent lawsuits, Novartis doubles down in Entresto defense with FDA complaint*, FIERCE PHARMA (Aug. 1, 2024), https://www.fiercepharma.com/pharma/novartis-sues-fda-over-approval-generic-version-its-bell-cow-entresto; Letter from Patrizia Cavazzoni, Dir., Ctr. Drug Eval. & Res., U.S. Food & Drug Admin., to David Platt, VP & Medical Head, Cardiovascular & Metabolism, U.S. Clinical Dev. & Medical Affs., Novartis Pharmaceuticals Corp. (July 24, 2024), https://www.regulations.gov/document/FDA-2022-P-2228-0015; Letter from Edward M. Sherwood, Dir., Off. Reg. Operations, Off. Generic Drugs, Ctr. Drug Eval. & Res., to Kondal Reddy Bairy, VP, MSN Pharmaceuticals Inc. (July 24, 2024), https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2024/213748Orig1s000ltr.pdf.

after the drug's approval.[187] These arguments are made in the face of the FDA's determination that these carveouts are permitted under law and would not make the generic products less safe or effective for the remaining conditions of use.[188]

In sum, Novartis has (1) unlawfully maintained monopoly control over Entresto with multiple patents, some of which could not and should not have covered the drug complex, (2) used crystalline patents to obtain additional protection on the drug, and (3) leveraged its method of use patents to try and block generics for nearly 21 years after the drug's approval.

Enbrel (Etanercept)

In a previous report, Public Citizen analyzed Amgen's patent gamesmanship to extend monopoly control on the drug etanercept (marketed as Enbrel).[189] We summarize that information below.

Etanercept is a biologic product that that treats autoimmune diseases like rheumatoid arthritis.[190] From June 2022 to May 2023, Medicare Part D spent almost $3 billion dollars covering the prescription's costs, which is approximately $60,000 per year for each Medicare enrollee prescribed the treatment. The average out-of-pocket cost for Part D patients without a low-income subsidy was more than $2,000 per year for just this drug.[191]

Amgen did not contribute to the research and development of etanercept, which was first approved in 1998. In 2002, Amgen acquired the smaller company, Immunex, which originally manufactured the drug, for $16 billion to secure the lucrative potential of Enbrel.[192] That company's patents covering etanercept were set to expire in 2019.[193] Using abusive patent practices, Amgen successfully thwarted competition from two potential biosimilar competitors, Erelzi and Eticovo, which received FDA approval in 2016 and

---

[187] Letter from Patrizia Cavazzoni, Dir., Ctr. Drug Eval. & Res., U.S. Food & Drug Admin., to David Platt, VP & Medical Head, Cardiovascular & Metabolism, U.S. Clinical Dev. & Medical Affs., Novartis Pharmaceuticals Corp., at 23 (July 24, 2024), https://www.regulations.gov/document/FDA-2022-P-2228-0015.

[188] Letter from Patrizia Cavazzoni, Dir., Ctr. Drug Eval. & Res., U.S. Food & Drug Admin., to David Platt, VP & Medical Head, Cardiovascular & Metabolism, U.S. Clinical Dev. & Medical Affs., Novartis Pharmaceuticals Corp., at 34, 38-42 (July 24, 2024), https://www.regulations.gov/document/FDA-2022-P-2228-0015.

[189] JISHIAN RAVINTHIRAN & STEVE KNIEVEL, USING THE INFLATION REDUCTION ACT TO REIN IN PHARMACEUTICAL COMPANY ABUSES: THE CASE OF ENBREL (2023).

[190] ASSISTANT SECRETARY PLANNING & EVALUATION, U.S. DEP'T HEALTH & HUMAN SERVS., INFLATION REDUCTION ACT RESEARCH SERIES: ENBREL: MEDICARE ENROLLEE USE AND SPENDING (Oct. 31, 2023), https://aspe.hhs.gov/sites/default/files/documents/9a83c694a036b1a1e55ff8763f674b8c/Enbrel.pdf.

[191] *Id.*

[192] Jonathan Gardner, *A three-decade monopoly: How Amgen built a patent thicket around its top-selling drug*, BIOPHARMA DIVE (Nov. 1, 2021), https://www.biopharmadive.com/news/amgen-enbrel-patent-thicket-monopoly-biosimilar/609042/; Justin Gillis, *Amgen Agrees to Buy Immunex in Record Biotech Deal*, WASH. POST (Dec. 18, 2001), https://www.washingtonpost.com/archive/business/2001/12/18/amgen-agrees-to-buy-immunex-in-record-biotech-deal/fff0293c-a412-4011-8322-49cf15855462/.

[193] Pet. for Writ of Cert. at 2, Sandoz, Inc. v. Immunex Corp., No. 20-110 (Jan. 29, 2021).

2019, respectively.[194] While Americans will be deprived of more affordable biosimilars until 2029, European peers have had access to these options since 2016.[195]

Patent Gamesmanship Hinging on Deceitful Contractual Practices

Etanercept helps treat symptoms of autoimmune diseases by inhibiting the protein, Tumor-Necrosis Factor (TNF), which is key to immune and inflammatory responses. The excessive or inappropriate production of the protein causes the harmful consequences associated with autoimmune diseases, like rheumatoid arthritis.[196] Etanercept, in particular, is a TNF receptor that binds to and inactivates TNF in order to treat such diseases.[197]

In 1999, Immunex, the original manufacturer of Enbrel, entered into a licensing agreement with the Swiss company Roche, which had also been working on TNF receptors.[198] In 1995, Roche had applied for two patents related to TNF receptors,[199] and the agreement gave Immunex license to those patent applications.[200] But in 2004, after acquiring Immunex, Amgen and these parties entered a new licensing agreement providing a lump-sum payment of approximately $45 million to Roche, eliminating Immunex's obligation to pay royalties, giving Immunex the exclusive right to prosecute the covered Roche patent applications, and providing Immunex the option to convert the license to a complete assignment of rights for a meager $50,000.[201]

Using the authority to prosecute Roche's patent applications, Immunex amended Roche's two patent applications to cover etanercept (the active ingredient in Enbrel), which Immunex had already claimed in its own patents.[202] By gaming the patent system through the licensing of Roche's duplicative patent applications, Amgen was able to win patent protection extending until 2029, a decade after the underlying protection from Immunex's patents was set to expire.[203]

---

[194] Gardner, *supra* note 192; Tony Hagen, *NJ Court Decision Means 3 Decades of Product Exclusivity for Enbrel*, CTR. BIOSIMILARS (Dec. 1, 2021), https://www.centerforbiosimilars.com/view/nj-court-decision-means-3-decades-of-product-exclusivity-for-enbrel.

[195] *See* Elif Car et al., *Biosimilar competition in European markets of TNF-alpha inhibitors: a comparative analysis of pricing, market share and utilization trends*, 14 FRONT PHARMACOL. 1 (2023); Press release, Samsung Bioepsis, Samsung Bioepis Enters into Commercialization Agreement for Next-Generation Biosimilar Candidates (Nov. 6, 2019), https://www.samsungbioepis.com/en/newsroom/newsroomView.do?idx=138.

[196] Dan-In Jang et al., *The Role of Tumor Necrosis Factor Alpha (TNF-α) in Autoimmune Disease and Current TNF-α Inhibitors in Therapeutics*, 22 INT. J. MOL. SCI. 2719 (2021).

[197] Mechanism of Action, ENBREL: ETANERCEPT, https://www.enbrelpro.com/more-about-enbrel/mechanism-of-action (last visited Aug. 26, 2024).

[198] Immunex Corp. v. Sandoz, Inc., 964 F.3d 1049, 1055 (Fed. Cir. 2020).

[199] Pet. for Writ of Cert. at 8, Sandoz, Inc. v. Immunex Corp., No. 20-110 (Jan. 29, 2021).

[200] *Immunex Corp*., 964 F.3d at 1055.

[201] *Id*. at 1055; *Immunex Corp*., 964 F.3d at 1069-70 (Reyna, J. dissenting).

[202] *Immunex Corp*., 964 F.3d at 1069 (Reyna, J. dissenting).

[203] Pet. for Writ of Cert. at 2, Sandoz, Inc. v. Immunex Corp., No. 20-110 (Jan. 29, 2021).

In patent law, a party is not allowed to extend the period of exclusivity for its invention with claims in a later-filed patent that are obvious variants of claims in an earlier patent owned by the same party.[204] But the courts ultimately found that the duplicative patents were not owned by the same party.[205] The Federal Circuit reasoned that the licensing agreement between Immunex and Roche did not transfer all of the substantial rights in the patent applications to Immunex to make it the effective owner of Roche's patents.[206] The technicality that Immunex owned the earlier patents and Roche owned the later patents meant that generic manufacturers could not invalidate the duplicative protection.[207] In consequence, two patent applications first filed by Roche in 1995 have enabled Amgen to preserve its monopoly until 2029.

The Federal Circuit's ruling prioritized form over substance: Immunex and Amgen are the effective owners of Roche's patents, and the reworked patents unfairly extend the drug's exclusivity, as Judge Reyna pointed out in dissent.[208] Any rights Roche retains are illusory since Immunex, at any time, can compel a complete assignment of Roche's patents for just $50,000.[209] Roche itself was willing to assign all rights to the patents for free, but Immunex was the party that insisted on the provision,[210] presumably to engage precisely in this sort of gamesmanship to undermine legal challenges to its monopoly. The $50,000 is a paltry sum to exercise the option of complete assignment, given that the entire agreement provided Roche $45 million, and Enbrel's sales were in the billions.[211] Due to the common ownership of the patents, the Court should have held the claims in the reworked Roche patents as invalid because they were obvious over the claims in Immunex's earlier patents.[212]

The Federal Circuit's illogical decision can be summed up by the fact that Amgen and Immunex are the effective owners of Roche's patents when they earn billions of dollars off Enbrel each year, but they are not effective owners of the patents for the purposes of law. Unfortunately, Amgen's patent gamesmanship found success again in a second district court ruling centering the same patents, which prevented a different biosimilar, Eticovo, from coming to market.[213]

---

[204] *Id.* at 1056; *Immunex Corp.*, 964 F.3d at 1068 (Reyna, J. dissenting).
[205] *Immunex Corp.*, 964 F.3d at 1056.
[206] *Id.* at 1061-63.
[207] *Id.* at 1063.
[208] *Immunex Corp.*, 964 F.3d at 1069-71 (Reyna, J. dissenting).
[209] *Id.* at 1069.
[210] *Id.* at 1070.
[211] *Id.*
[212] *Id.* at 1071-72.
[213] Immunex Corp. v. Samsung Bioepis Co., No. 2:19-cv-11755-CCC-LDW (D. N.J. Nov. 3, 2021); Tony Hagen, *NJ Court Decision Means 3 Decades of Product Exclusivity for Enbrel*, CTR. BIOSIMILARS (Dec. 1, 2021), https://www.centerforbiosimilars.com/view/nj-court-decision-means-3-decades-of-product-exclusivity-for-enbrel.

CONCLUSION

It is no surprise that nine out of 10 drugs selected for Medicare price negotiation exemplify patterns of patenting designed to unfairly extend market exclusivity on some of the most lucrative drugs in the world. These tactics have had, and will continue to inflict, significant financial consequences on families and patients as they delay and hamper access to more affordable treatments. The Inflation Reduction Act provides the government a powerful tool to remedy the harms and exploitation of American patients by the pharmaceutical industry. We urge CMS to account for unfair monopoly extensions that exact huge financial tolls on patients and Medicare in arriving at maximum fair prices for enrollees during the negotiation process.

Public Citizen's analysis shows that, were it not for patent abuses and evergreening practices, biosimilar and generic competitors would already have entered the market by the time negotiated prices go into effect for four of the 10 selected drugs. As a result, Medicare will lose between $4.9 billion and $5.4 billion in savings by the time negotiated prices go into effect due to these tactics that have prevented timely access to generics and biosimilars for U.S. patients. Analysis from the Brookings Institute shows that CMS negotiated steeper discounts for three of the four drugs that should have faced price competition before negotiated prices go into effect (Stelara, Enbrel, and Januvia).[214] We commend CMS for obtaining more significant savings on drugs subject to patenting tactics that have deprived Medicare enrollees of generics and biosimilars to date. However, this could also be a consequence of heightened leverage for CMS due to a lower statutorily prescribed ceiling on the maximum fair price for long-monopoly drugs like Stelara, Enbrel, and Januvia.

But even with more significant savings from negotiations on these drugs, the anticipated savings CMS will obtain in the first year if negotiated prices go into effect for all of the selected drugs ($ 6 billion) are almost erased by how much taxpayers have already lost due to the patent abuses and evergreening practices on Enbrel, Stelara, Januvia, and Xarelto.[215] In future years, we urge CMS to weight these patenting tactics more heavily in negotiating maximum fair prices. Specifically, with respect to long-monopoly drugs, CMS should consider how manufacturers have managed to obtain lengthy exclusivities on these drugs by manipulating patents and exclusivities in developing initial offers.

Further, this report highlights how pharmaceutical corporations have used a number of patenting tactics on almost all of the drugs (9 out of 10) subject to the first round of Medicare drug price negotiation to extend monopoly control on these medicines. These

---

[214] ANNA ANDERSON-COOK & RICHARD G. FRANK, BROOKINGS INST., IMPACT OF FEDERAL NEGOTIATION OF PRESCRIPTION DRUG PRICES (Aug. 19, 2024), https://www.brookings.edu/articles/impact-of-federal-negotiation-of-prescription-drug-prices/.

[215] CTRS. MEDICARE & MEDICAID SERVS., MEDICARE DRUG PRICE NEGOTIATION PROGRAM: NEGOTIATED PRICES FOR INITIAL PRICE APPLICABILITY YEAR 2026, at 4 (Aug. 2024), https://www.cms.gov/files/document/fact-sheet-negotiated-prices-initial-price-applicability-year-2026.pdf.

practices include obtaining later-expiring patents on previously known information, claiming obvious forms of drug compounds that would have been discovered during the drug approval process, patenting methods of screening patients to check drug safety and efficacy, and deploying licensed and acquired patents to block competitors from innovating more affordable treatment options.

The Inflation Reduction Act provides an elegant fix to the rampant and complex patent abuses that enable price gouging on these drugs: negotiate maximum fair prices that account for these patents and the revenues these companies unfairly obtain through extended monopoly control on these drugs. Only then can the prices for Medicare enrollees be fair.

Other Recommendations

Public Citizen also endorses the below recommendations, many of which were proposed by the Initiative for Medicines, Access, and Knowledge.

1) **Reject the PREVAIL Act and any other attempts to make it harder for generic firms to challenge evergreening and patent abuse by branded manufacturers before the Patent Trial and Appeal Board.**

The PREVAIL Act advanced favorably out of the Senate Judiciary Committee on November 21, 2024. That bill would heighten the standard for invalidating problematic patents at PTAB by raising the burden of proof for proving patent invalidity.[216] It would also limit effective review of petitions. Alarmingly, the bill requires PTAB to reject institution where a challenge presents prior art that is the same or substantially same as prior art that was presented to the PTO during patent examination.[217] Branded manufacturers will predictably inundate resource-constrained PTO examiners with hundreds, if not thousands, of prior art documents that can effectively preempt PTAB challenges by generic firms.[218] Further, the bill may limit the efficacy of PTAB challenges by requiring manufacturers to challenge any and all weak patent claims in a single petition under threat of forfeiting unraised claims about patent invalidity in other proceedings.[219] Combined with the word limit on PTAB petitions, manufacturers may be

[216] Promoting and Respecting Economically Vital American Innovation Leadership Act, S. 2220 §§ 4(e)(2), 5(d)(2) (raising the burden of proof for proving unpatentability to "clear and convincing" evidence).
[217] Promoting and Respecting Economically Vital American Innovation Leadership Act, S. 2220 §§ 4(e)(2).
[218] Wayne Brough, *Coalition Letter in opposition to the Promoting and Respecting Economically Vital American Innovation Leadership Act ("PREVAIL Act")*, R ST. INST. (Sept. 16, 2024), https://www.rstreet.org/outreach/coalition-letter-in-opposition-to-the-promoting-and-respecting-economically-vital-american-innovation-leadership-act-prevail-act/.
[219] Promoting and Respecting Economically Vital American Innovation Leadership Act, S. 2220 §§ 4(d) & 5(c).

unable to comprehensively challenge bad patent claims granted to branded manufacturers.[220]

By limiting the effectiveness of PTAB challenges and making it harder to win them by raising the evidentiary standard, the PREVAIL Act will place biosimilar and generic manufacturers at a disadvantage in challenging evergreening and patent abuses by branded manufacturers. Branded manufacturers, emboldened by the effects of the PREVAIL Act in insulating their patent gaming tactics from invalidation, will refuse to settle with competitors to allow generic and biosimilar entry to the market. Currently, nearly **one in four** petitions challenging small molecule drug patents and **one in five** petitions challenging biologic patents result in settlement.[221] In light of the widespread patent abuses detailed in this report, some of those settlements likely arise from branded manufacturers' awareness of the weaknesses in their patent claims. The PREVAIL Act's overhaul of PTAB to favor originators, though, will ultimately undercut these settlements that benefit U.S. patients. In sum, the heightened protection of branded manufacturers' patents due to this bill will allow them to maintain monopoly prices longer, thereby hurting U.S. patients. This would contravene the aims and purposes of the Affordable Prescriptions for Patients Act recently passed by the Senate to curtail patent abuses by branded manufacturers.

Additionally, in the area of pharmaceutical and biologic patents, the PREVAIL Act attempts to solve a non-existent problem regarding increased patent invalidation at PTAB, all while imposing significant harms on patient access. The Patent and Trademark Office (PTO), in its comprehensive review of petitions before PTAB between 2012 and March 2024, found that institution was denied for 32% of petitions challenging small molecule drug patents.[222] Only 15% of the petitions challenging these patents resulted in final written decisions invalidating all of the patent claims.[223] Further, PTAB found all claims patentable in 15% of petitions challenging these patents. Only 2% resulted in a mixed outcome.[224] In total, of the 6,619 small molecule drug patent claims challenged during this nearly 12 year period, PTAB only held 933 claims unpatentable.[225] For petitions challenging biologic patents, PTAB denied institution for 39% of the petitions, found all the patent claims invalid in 22% of the petitions, found all the claims valid in 6% of the petitions, and provided a mixed outcome in 3% of the cases.[226] In total, of the 3,449 biologic

[220] Wayne Brough, *Coalition Letter in opposition to the Promoting and Respecting Economically Vital American Innovation Leadership Act ("PREVAIL Act")*, R ST. INST. (Sept. 16, 2024), https://www.rstreet.org/outreach/coalition-letter-in-opposition-to-the-promoting-and-respecting-economically-vital-american-innovation-leadership-act-prevail-act/.
[221] U.S. PAT. & TRADEMARK OFF., PTAB ORANGE BOOK PATENT/BIOLOGIC PATENT STUDY FY24 Q2 UPDATE (THROUGH MARCH 31, 2024) 13-14 (2024).
[222] *Id*.
[223] *Id*.
[224] *Id*.
[225] *Id*.
[226] *Id*.

patent claims challenged, PTAB held 787 claims invalid.[227] This data shows PTAB invalidates claims in pharmaceutical and biologic patents in a minority of cases, and when it does so, the Board likely has good reason based on pervasive patent gaming tactics by drugmakers as detailed in this report. If anything, PTAB should be holding their patents to higher standards to combat these abuses.

More generally, concerns about multiple petitions at PTAB that the PREVAIL Act is theoretically designed to deter are exaggerated based on PTO's empirical data. PTO shows that only 1.7% of petitions represent serial petitions (petitions filed by the same petitioner against the same patent more than 90 days apart) and only 0.3% of all challenges resulted in institution for a serial petition.[228] The reasons for institution were also rational: (1) the patent owner did not contest the challenge, (2) new claims were asserted in district court, (3) the serial petition was filed after new guidance on *inter partes* review was released, (4) there was a large number of claims in the patent, or (5) there was a dismissal of the International Trade Commission proceeding used to deny institution of the original petition.[229] In 2019, parties were also required to justify why two or more petitions challenging the same patent were necessary.[230] PTO shows that only 7% of petitions represent parallel petitions (the petition is filed 90 days or fewer apart by the same petitioner against the same patent).[231] Further, only 3.4% of all petitions resulted in institution on parallel petitions.[232] Again, there were justifiable bases for institution on a parallel petition: (1) there was a large number of claims/complex claim set, (2) there were prior art eligibility issues, (3) priority date issues, (4) different claims at issue, or (5) the patent owners did not oppose the parallel petition.[233] Thus, the PREVAIL Act introduces a number of challenges for generic and biosimilar manufacturers and nonprofits seeking to challenge verifiable patent abuses, which are not counterbalanced by fixing an alleged problem of multiple petitions against the same patent. Discretion at PTAB already screens out the vast majority of unmeritorious challenges by potential abusers.

Amendments offered to resolve concerns about the Act are insufficient. The Act's provisions can still be read literally to deprive generic firms of standing to institute PTAB proceedings because the petition cannot be for "profit. . .or fund the operations of the petitioner,"[234] which are obviously incidental motivators for these firms. Further, amendments to ensure nonprofits can continue to use PTAB will be ineffective given the kind of information collection from donors and members necessary to demonstrate standing. The bill makes nonprofits' standing contingent on not having "any member,

[227] *Id*.
[228] U.S. PAT. & TRADEMARK OFF., PATENT TRIAL AND APPEAL BOARD MULTIPLE PETITIONS STUDY (FISCAL YEARS 2021-2022 UPDATE) 6-9 (July 2023).
[229] *Id*.
[230] *Id*. at 11-15.
[231] *Id*.
[232] *Id*.
[233] *Id*.
[234] Promoting and Respecting Economically Vital American Innovation Leadership Act, S. 2220 § 4(b)(3).

donor, or other funding source that is, or reasonably could be accused of, infringing 1 or more claims of the challenged patent." For nonprofits with thousands of members and small donors, certifying that no individual could reasonably be accused of infringing the patent claims would be impossible without extreme data collection. Given these organizations' resource limitations, these organizations simply would never bring PTAB challenges. In short, the PREVAIL Act is highly likely to aggravate the drug pricing crisis in the United States.

2) **Where a prior patent covering a drug compound discloses or claims a therapeutic application, a subsequent patent claim on the same indication should be obvious and unpatentable.**

There is some case law that already exists to prevent subsequent patent claims on previously disclosed information and knowledge. For example, the Federal Circuit has previously affirmed decisions invalidating claims in method of use patents covering a use that has been previously disclosed in a patent covering the same composition.[235] In applying the law, however, lower courts can escape the applicability of these precedents by finding that subsequent method of use patents do not cover the exact same composition. In Januvia's case, the district court refused to invalidate the method of use claim because the earlier patent covered a more general class of compounds, while the later patent covered a more specific compound within that class, even though the patents shared the exact same therapeutic application.[236]

These rulings highlight how patenting standards are too lenient in the United States. Congress must consider ambitious patent reforms that anticipate how pharmaceutical companies can use marginal variations in drug patents to escape rules and reforms designed to limit evergreening abuses. Thus, we support I-MAK's proposal that "Congress should pass legislation whereby a secondary patent claiming a method of use for an indication which has already been disclosed and/ or claimed in a primary patent relating to a product is obvious and, therefore, unpatentable."[237] Congress may consider adding text that provides for liberal construal of these provisions to prevent lower courts from narrowing the ambit of these proposals. Further, PTO should be empowered to promulgate rules and guidance to ensure narrower versions of an indication or marginal variations of a drug compound do not thwart such patent reform.

Some may argue that this reform would discourage research and development of therapeutic applications previously disclosed for drug compounds; that criticism obscures that the FDA already provides three years of clinical data exclusivity for these

[235] Merck Sharp & Dohme, LLC v. Mylan Pharm., No. 1:19CV101, at 97-99 (N.D. W.Va. Sep. 21, 2022) (discussing the Federal Circuit's decision in Pfizer Inc. v. Teva Pharms. USA, Inc., 518 F.3d 1353 (Fed. Cir. 2008))

[236] *Id*.

[237] I-MAK, ADDRESSING PATENT THICKETS TO IMPROVE COMPETITION AND LOWER PRESCRIPTION DRUG PRICE: A BLUEPRINT FOR REFORM 5 (2023).

kinds of studies and that market exclusivity, which can be worth billions, is already sufficient to advance that kind of research.

3) **Patents covering a crystalline/polymorph version of a previously claimed or disclosed compound should be declared obvious and unpatentable.**

Many of the drugs subject to the first round of negotiation, including Eliquis, Imbruvica, Jardiance, Farxiga, and Entresto, had patents on crystalline forms of the drug compound to extend or expand monopoly protections on the drug. These crystalline forms, and their different crystal structures (polymorphs), can differ in important therapeutic properties for patients, which is why the FDA promulgated guidance recommending routine testing to monitor and manage these forms to obtain marketing authorization.[238] In some cases, like Imbruvica, there is no question that an inventor would have been motivated to discover the most stable version of the drug compound, which was a crystalline form of the drug for which the manufacturer obtained a later-expiring patent.[239] These kinds of obvious patents are not invalidated typically because lower courts rely on the "unpredictable nature" of creating crystalline forms of a drug.[240] The common practice of extending and expanding monopoly control on the drugs through crystalline patents and the FDA's guidance on monitoring their forms suggests that caselaw currently departs from reality: Congress must pass legislation to prevent the pharmaceutical industry from unfairly extending exclusivity on drugs through crystalline/polymorph patents.

4) **Restricting acquired and licensed patents that can be asserted in patent litigation, particularly for biologics.**

We found particularly egregious patenting practices to extend exclusivities on Enbrel and Stelara, both biologic products. These include deploying recently acquired patents on biosimilar manufacturing, with no relevance to producing the reference branded drug, to deprive U.S. patients of more affordable alternatives and using licensed patents to circumvent legal limits on indistinct patent claims.

Recent legislation passed in the Senate seeks to constrain at least some of these kind of practices by limiting patents asserted in infringement actions that claim a method in a manufacturing process that is not used by the reference product sponsor.[241] That bill, the Affordable Prescriptions for Patients Act of 2023, would have limited Johnson & Johnson's ability to assert the biosimilar manufacturing patents against other companies within a cap of 20 patents including other categories of patents typically used to build patent

[238] I-MAK, ADDRESSING PATENT THICKETS TO IMPROVE COMPETITION AND LOWER PRESCRIPTION DRUG PRICE: A BLUEPRINT FOR REFORM 7 (2023).
[239] Pharmacyclics, LLC v. Alvogen, Inc., Case No. 21-2270, at 22-23 (Fed. Cir. 2022), https://cafc.uscourts.gov/opinions-orders/21-2270.OPINION.11-15-2022_2033497.pdf.
[240] I-MAK, ADDRESSING PATENT THICKETS TO IMPROVE COMPETITION AND LOWER PRESCRIPTION DRUG PRICE: A BLUEPRINT FOR REFORM 7 (2023).
[241] S. 150, Affordable Prescriptions for Patients Act of 2023, 118 Cong., https://www.congress.gov/bill/118th-congress/senate-bill/150/text?s=1&r=1&q=%7B%22search%22%3A%22S.150%22%7D.

thickets. [242] Ultimately, however, the bill would not have prevented this plain abuse of the patent system if Johnson & Johnson did choose to assert these unmerited patents within the cap. Thus, these reforms must go further to address the harms of these kind of patenting practices on U.S. patients. As we stated previously, it is challenging to articulate any pro-innovation effects or benefits to consumers by allowing branded manufacturers to acquire and assert biosimilar manufacturing patents solely for the purpose of blocking competitors from innovating their own more affordable options. Rather than just seeking to limit the number of these patents that can be asserted in litigation, Congress must prohibit this practice.

Further, Congress should explore legislation to close loopholes that allow drug corporations to evade appropriate scrutiny over their patents through deceitful licensing arrangements and inappropriately extend monopolies by patenting obvious inventions. This can include restricting or banning certain patents from being asserted in litigation for biologics if they have been granted a certain number of years after the drug's approval, which is similar to provisions in the bill the Senate passed. In Enbrel's case, however, the licensed patents were filed before the drug's approval in 1998 but were granted after 2010 to extend monopoly control over the drug until 2029. It is highly suspect that patents covering a biologic can be granted more than 12 to 13 years after the biologic's approval to extend exclusivity for another decade. To address the clear anticompetitive abuses on Enbrel in the future, Congress may seek to limit or prohibit patents granted a certain number years after a biologic's approval from being asserted in patent litigation, unless that patent has clear and convincing evidence of additional therapeutic value to patients.

[242] Tahir Amin, *Why Current Legislative Efforts to Prevent Patent Thickets Are a Start — But Not Enough*, MEDIUM (Apr. 3, 2024), https://medium.com/@realtahiramin/why-current-legislative-efforts-to-prevent-patent-thickets-are-a-start-but-not-enough-aab87ec58446.

APPENDIX: METHODOLOGY FOR CALCULATING MEDICARE'S LOSSES DUE TO PATENTING AND EVERGREENING ABUSES BY 2026

First, using available data from the Orange Book and litigation documents, we determined when Stelara, Januvia, and Xarelto would likely have faced biosimilar and generic competition were it not for evergreening tactics or patent abuses. For Xarelto, we determined the relevant patents would have expired by May 13, 2025.[243] For Januvia, this date would have been January 26, 2023.[244] For Stelara, patent protection was expected to expire in September 2023.[245] We verified that a generic or biosimilar obtained tentative or final approval from the FDA by these dates to project savings for the drugs. For Stelara, however, the first biosimilar was approved October 31, 2023.[246]

Second, we estimated the period during which savings would accrue if generic or biosimilar competition had occurred were it not for the evergreening tactics or patent abuses. Our analysis examines the savings that should have accrued before negotiated prices go into effect on January 1, 2026. However, we did not apply this endpoint to Stelara because public information suggests that Amgen will be able to market its biosimilar no later than January 1, 2025 pursuant to a confidential settlement agreement with Johnson & Johnson.[247] Therefore, to estimate the savings that would have accrued due to generic or biosimilar competition before negotiated prices go into effect, we projected savings from February 2023 through December 2025 for Januvia; savings from November 2023 through December 2024 for Stelara; and June 2025 through December 2025 for Xarelto.

---

[243] *See* Xarelto (Rivaroxaban) (discussing how two patents expire by May 13, 2025, which we use as the cut off here, because the patent covering the once daily regimen expiring in 2034 constitutes an evergreening abuse and the patent covering the 2.5 mg coadministration with aspirin was invalidated); U.S. Food & Drug Admin., *Product Details for NDA 022406*, ORANGE BOOK: APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS, https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=N&Appl_No=022406#23884 (last visited Aug. 20, 2024).

[244] Merck Sharp & Dohme, LLC v. Mylan Pharm., No. 1:19CV101 10-11, at 16-17 (N.D.W. Va. Sep. 21, 2022).

[245] CareFirst of Maryland v. Johnson & Johnson, Civil Action No. 2:23-cv-00629-JKW-LRL, at 51-54 (D.Va. Feb. 5, 2024), https://www.hbsslaw.com/sites/default/files/case-downloads/stelara-antitrust/2024-02-05-amended-complaint.pdf; *see also* Jonathan Gardner, *Acquired patents aid J&J defense of top-selling drug from biosimilar challenge,* BIOPHARMA DIVE (Mar. 29, 2023), https://www.biopharmadive.com/news/johnson-johnson-stelara-patents-amgen-biosimilar-momenta/646277/; Johnson & Johnson, 2021 Form 10-K at 3, https://www.sec.gov/ix?doc=/Archives/edgar/data/0000200406/000020040621000008/jnj-20210103.htm.

[246] Press Release, U.S. Food & Drug Admin., FDA Approves Interchangeable Biosimilar for Multiple Inflammatory Diseases (Oct. 31, 2023), https://www.fda.gov/news-events/press-announcements/fda-approves-interchangeable-biosimilar-multiple-inflammatory-diseases.

[247] Blake Brittain, *Amgen settles patent lawsuit over biosimilar of J&J's big-selling Stelara*, REUTERS (May 23, 2023), https://www.reuters.com/business/healthcare-pharmaceuticals/amgen-settles-jj-patent-lawsuit-over-drug-similar-blockbuster-stelara-2023-05-23/.

We estimated gross spending by Medicare Part D for these drugs during these time periods using the historical data from Medicare and, for future years, we projected forward the latest expenditure data for Fiscal Year 2022. We attempted to account for U.S. market trends by decreasing or increasing the gross expenditure based on revenue changes from Fiscal Year 2022 to Fiscal Year 2023 disclosed for U.S. Sales in filings with the Securities Exchange Commission, and projecting that forward into future years. Between Fiscal Year 2022 and Fiscal Year 2023, Xarelto's U.S. sales decreased by 4.4%.[248] For Januvia, U.S. sales decreased by 7.8% between 2022 and 2023.[249] Finally, for Stelara, U.S. sales increased by 9% over the same period.[250] Although there is inherent uncertainty in projecting spending in future years, we believe the approach used here is more conservative than simply projecting forward the latest spending period's data, given that Medicare spent more on Xarelto and Januvia compared to Stelara.

After estimating gross expenditure by Medicare Part D from February 2023 through December 2025 for Januvia; from November 2023 through December 2024 for Stelara; and June 2025 through December 2025 for Xarelto, we calculated net expenditure by Medicare during these periods by factoring in potential rebates and discounts from the manufacturer. We used estimated rebate percentages as reported by the Commonwealth Fund. For Stelara, rebates accounted for 29% of expenditures; for Xarelto, rebates accounted for 49% of expenditures; and for Januvia, rebates accounted for 50% of expenditures.[251]

Next, we used different savings calculations for small molecule drugs versus biologics. These calculations in lost savings to Medicare do not account for potential increased usage of Xarelto, Januvia, and Stelara and their generic and biosimilar competitors due to lower prices for these treatments arising from competition. Such usage, however, would indicate that Medicare enrollees currently are depriving themselves of necessary treatment due to cost barriers imposed by the manufacturers and marketers.

Savings Calculations for Xarelto & Januvia

For small molecule drugs, the FDA has readily available data on price reductions compared to the originator as a function of the number of generic competitors. With six or more competitors, the FDA finds that prices decrease by 95% compared to brand

[248] Johnson & Johnson, Form 10-K (2023) at 84, https://www.sec.gov/ix?doc=/Archives/edgar/data/200406/000020040624000013/jnj-20231231.htm.
[249] Merck, Form 10-K (2023), at 124, https://www.sec.gov/ix?doc=/Archives/edgar/data/310158/000162828024006850/mrk-20231231.htm.
[250] Johnson & Johnson, 10-K Form (2023) at 84, https://www.sec.gov/ix?doc=/Archives/edgar/data/200406/000020040624000013/jnj-20231231.htm
[251] EVAN D. GUMAS, PAIGE HUFFMAN, IRENE PAPANICOLAS, & REGINALD D. WILLIAMS II, COMMON WEALTH FUND, HOW PRICES FOR THE FIRST 10 DRUGS UP FOR U.S. MEDICARE PRICE NEGOTIATIONS COMPARE INTERNATIONALLY (Jan. 4, 2024), https://www.commonwealthfund.org/publications/2024/jan/how-prices-first-10-drugs-medicare-negotiations-compare-internationally.

prices.[252] Experts have separately found large price decreases as a function of number of generic competitors: with 10 generic manufacturers or more, prices fell 89% compared to the brand level.[253] Recent estimates from the Congressional Budget Office suggest that four years after the first generic product enters the market, there is a 60% price reduction for generics in Medicare Part D compared to the net price of the brand-name drug.[254] Researchers also find that in the first year of generic competition for a drug, there is 66.1% uptake of generics; in the second year, uptake of generics increases to 82.7%.

For Xarelto and Januvia, there were ten generic manufacturers with tentatively approved generics when patent protection would have expired according to the FDA's drug database.[255] Given the range of price reductions of generics compared to brand prices in the literature, we chose the more conservative figure of a 60% price reduction from CBO. Some may criticize the use of CBO's figure given that the analysis was conducted using prices four years from first generic entry in Medicare Part D. If more precise data was available on price reductions of generics in Medicare Part D compared to brand prices as a function of the number of generic manufacturers immediately after their market entry, we would have used such information. In its absence, we expect CBO's figures to underestimate the effect of robust generic competition on these two lucrative drugs, as the 60% price reduction is an aggregate figure across Medicare Part D drugs regardless of the number of generic competitors.

For Xarelto, we assumed 66.1% generic uptake for the period of June 2025 through December 2025 with a 60% price reduction for generics compared to the originator. For Januvia, we assumed 66.1% uptake from February 2023 to January 2024, 82.7% generic uptake from February 2024 to January 2025, and 82.7% generic uptake from January 2025 to December 2025, with a 60% price reduction for generics compared to the originator. Although we would expect generic uptake to increase in that third year, to be conservative, we assumed 82.7% uptake of generics in that year, too.

Using these figures, we calculated the net expenditure that would remain for the branded drug's share of the market in each year and the net expenditure on generics that would occur as a function of their market share given a 60% price reduction compared to the brand price. We totaled this amount to understand how much Medicare would have spent with likely generic entry were it not for evergreening tactics. Then we compared this to

---

[252] RYAN CONRAD & RANDALL LUTTER, FOOD & DRUG ADMIN., GENERIC COMPETITION AND DRUG PRICES: NEW EVIDENCE LINKING GREATER GENERIC COMPETITION AND LOWER GENERIC DRUG PRICES 3 (Dec. 2019).
[253] Chintan V. Dave, Abraham Hartzema, & Aaron Kesselheim, *Prices of Generic Drugs Associated with Numbers of Manufacturers*, 377 N. ENGL. J MED. 2597 (Dec. 2017).
[254] Cong. Budget Off., Alternative Approaches to Reducing Prescription Drug Prices 12 (Oct. 2024),
[255] U.S. Food & Drug Admin., *Search Results for "sitagliptin phosphate,"* DRUGS@FDA: FDA- APPROVED DRUGS, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process (last visited Aug. 26, 2024); U.S. Food & Drug Admin., *Search Results for "rivaroxaban,"* DRUGS@FDA: FDA- APPROVED DRUGS, https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process (last visited Aug. 26, 2024).

Medicare's projected net expenditures without generics until negotiated prices go into effect. The difference was the lost savings to Medicare due to evergreening tactics which likely delay and deprive enrollees of lower-cost alternatives.

For Januvia, we found Medicare Part D will likely spend $5,082,525,470.69 on a net basis between February 2023 and December 2025. If Januvia faced generic competition during this time period, we found that Medicare Part D would likely spend $2,747,575,497.53 on a net basis for both the branded medication and its generics. That is, Medicare will likely lose $ $2,334,949,973.16 in savings because of Merck's evergreening tactics on Januvia that delay and deprive Medicare patients of generics.

For Xarelto, we found that Medicare Part D will likely spend $1,500,508,024.36 on a net basis between June 2025 and December 2025. With generic competition, we found that Medicare Part D's likely net spend would be $905,406,541.90. As such, Medicare will lose $595,101,482.46 in savings because evergreening abuses prevent enrollees from accessing lower-cost alternatives to Xarelto during this period.

Savings Calculations for Stelara

Compared to estimating savings from generic competition on small molecule drugs, there is greater uncertainty for projecting biosimilar uptake and related price reductions compared to the brand name biologic. Therefore, to project how much Medicare would have saved were it not for patent abuses that delayed likely biosimilar competition, we used methods from the RAND Corporation to provide a lower bound and upper bound estimate of this figure. RAND calculated estimated savings under an "upper-bound" set of assumptions where the biosimilar market share is 50% and there is a 50% price reduction relative to the branded biologic. Under the "lower-bound" set of assumptions, RAND estimates cost savings where biosimilar uptake is 20% and the price reduction relative to the reference product is 20%.

From November 2023 through December 2024, we estimate that Medicare will likely have spent $2,274,838,249.82 on a net basis for Stelara. Using the lower-bound set of assumptions, Medicare would have spent $2,183,844,719.82 during this period if patients had access to a biosimilar alternative. Thus, were it not for Johnson & Johnson's patent abuses, likely biosimilar competition would have enabled Medicare to save at least $90,993,529.99 on a net basis before negotiated prices go into effect. Using the upper-bound set of assumptions, Medicare would have spent $1,706,128,687.36 if enrollees could have used a lower-cost biosimilar alternative during this time period. That is, Medicare could have saved as much as $568,709,562.45 in net spending had Medicare Part D enrollees been able to use lower-cost biosimilars were it not for Johnson and Johnson's patent abuses.

Aggregate Savings Calculations

In a prior publication, we had already estimated lost savings to Medicare due to Amgen's patent abuses on Enbrel before negotiated prices go into effect.[256] Enbrel is also a biologic, but we had more precise data available on price reductions from biosimilar uptake in Europe to calculate estimated lost savings. In that report, we estimated that biosimilars could have entered the market after August 2019 were it not for Amgen's unwarranted patent exclusivities, and we calculated Medicare would have spent $1,891,500,836 less on a net basis had enrollees been able to use lower-cost alternatives by the time negotiated prices go into effect on January 1, 2026. Thus, we aggregated the lost savings for Enbrel with Stelara, Xarelto, and Januvia to calculate the total lost savings to Medicare due to evergreening tactics and patent abuses before these prices go into effect. Medicare Part D would have spent $4,912,545,821.61to $5,390,261,854.07 less on a net basis on the drugs selected for price negotiation were it not for evergreening tactics and patent abuses by the time negotiated prices go into effect.

[256] JISHIAN RAVINTHIRAN & STEVE KNIEVEL, USING THE INFLATION REDUCTION ACT TO REIN IN PHARMACEUTICAL COMPANY ABUSES: THE CASE OF ENBREL (2023).