

Humira: The First \$20 Billion Drug

Jason B. Gibbons, PhD; Micaela Laber, MPH, MBA; and Charles L. Bennett, MD, PhD, MPP

AbbVie's adalimumab (Humira) is the top-selling pharmaceutical in the world, indicated for many autoimmune, rheumatologic, and gastrointestinal diseases. From 2011 to 2021, worldwide net revenues more than doubled from \$7.9 billion to \$20.7 billion as the drug's market power strengthened.¹ Due to concerns about government health program spending on Humira, in 2019, the US House Committee on Oversight and Accountability opened an investigation into AbbVie's pricing, patent, and marketing practices. Following a review of internal business documents, the Oversight Committee published majority staff reports^{2,3} identifying strategies that AbbVie used to extend market exclusivity for Humira beyond the usual US patent protection timeline (Figure). Although these strategies are not unique to AbbVie or Humira, we review these reports and describe policy debates surrounding the highest-grossing drug to highlight how the legal landscape enables incumbent manufacturers to block competition in the pharmaceutical market.

Review of AbbVie's Pricing Tactics

A significant factor in Humira's success has been the absence of biosimilar competition. This is partially related to Paragraph IV settlement agreements negotiated between AbbVie and adalimumab biosimilar manufacturers. Biosimilar manufacturers attempted to invalidate AbbVie's Humira patents so they could enter the US market before the technical end of its market exclusivity period, which in the United States was 2039.⁴ Biosimilar manufacturers ultimately dropped their patent cases and negotiated individual settlement agreements with AbbVie, in which they agreed not to contest AbbVie's patents in the United States and to delay US biosimilar adalimumab entry to 2023 in exchange for AbbVie agreeing not to fight entry of adalimumab biosimilars in the European Union.⁴ These agreements are often considered anticompetitive by regulators, as they are thought to extend market exclusivity of the biologic. Notably, although no adalimumab biosimilars have launched in the United States as of the end of 2022, other therapeutic alternatives considered competition to Humira have been on the market for several years. Still, AbbVie successfully increased Humira net revenues and increased its list and net prices despite the presence of competitor products.

ABSTRACT

AbbVie's adalimumab (Humira) is the top-selling pharmaceutical in the world. Due to concerns about government health program spending on Humira, the US House Committee on Oversight and Accountability opened an investigation in 2019 to investigate AbbVie's pricing and marketing practices. We review these reports and describe policy debates surrounding the highest-grossing drug to highlight how the legal landscape enables incumbent manufacturers to block competition in the pharmaceutical market. Tactics include patent thickets, evergreening, Paragraph IV settlement agreements, product hopping, and linking executive compensation to sales growth. These strategies are not unique to AbbVie and shed light on pharmaceutical market dynamics that may be hindering a competitive market. Policy reform and legal initiatives may help reduce anticompetitive behaviors by pharmaceutical manufacturers and increase access to competitive therapeutic options such as biosimilars.

Am J Manag Care. 2023;29(2):78-80. doi:10.37765/ajmc.2023.89315

A key barrier to biosimilar entry for Humira is AbbVie’s practices around patent protection. A review of AbbVie’s materials revealed that they employed evergreening and patent thicket strategies to extend their product’s patent life well beyond the originally granted exclusivity period.^{2,3} A patent thicket is when a manufacturer files many patents on one innovator product to deter competitors from legally challenging the patents of the innovator product. Since its original patent approval, AbbVie obtained or applied for 250 patents for Humira.³ Evergreening is when a manufacturer obtains secondary patents near primary patent expiration to extend market exclusivity. Some secondary patents obtained were specific to orphan and pediatric designations, which offer extended patent protection periods.

AbbVie also employed “product hopping,” whereby providers were encouraged to prescribe a less painful high-concentration formulation that is slightly different from Humira. AbbVie also transitioned providers and patients to new formulations of Humira, the line-extended products risankizumab (Skyrizi) and upadacitinib (Rinvoq). As biosimilars launch in 2023, this product hopping may affect market penetration of adalimumab biosimilars as patients transition to line-extended products that are considered imperfect substitutes.

AbbVie shifted patient and prescriber demand for Humira through its marketing tactics. In March 2021 alone, AbbVie spent \$40.5 million in television advertising for Humira, Skyrizi, and Rinvoq.⁴ AbbVie promoted financial assistance programs to patients to maintain brand loyalty. Internal documents revealed that 40% of Humira revenues went to funding marketing costs and patient assistance programs and 3% went to research and development.³

Most notably, AbbVie increased the list price of Humira 27 times since 2003. Between 2009 and 2018, the annual price for a biweekly

TAKEAWAY POINTS

In this article, we review a House Committee on Oversight and Accountability investigation report on AbbVie’s practices pertaining to adalimumab (Humira) to shed light on broader pharmaceutical market dynamics hindering a competitive market.

An understanding of pharmaceutical pricing and marketing strategies can help inform:

- ▶ Coverage and payment decisions for health plans
- ▶ Bipartisan policy options to enhance biosimilar competition
- ▶ Preparation for potential policy changes coming from Congress and courts to improve pharmaceutical competition

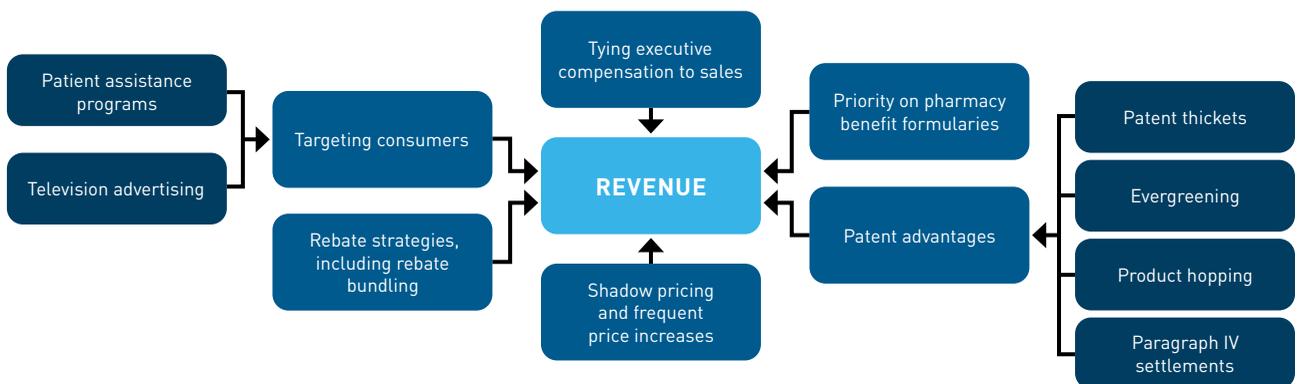
dose increased from \$16,663 to \$35,041.³ AbbVie engaged in a practice known as shadow pricing^{2,3} when it increased prices alongside an alternative drug from another company. Specifically, AbbVie’s Humira prices increased almost identically with prices of etanercept (Enbrel), a drug manufactured by Amgen but in the same therapeutic category.³ AbbVie also leveraged rebating strategies and established priority tiering on pharmacy benefit manager formularies.² This practice and other strategies such as rebate bundling have huge implications for the uptake of biosimilars across product classes because they increase use of brand biologics over biosimilars.

The final tactic AbbVie used was linking executive compensation to sales growth.^{2,3} This created incentives for executives to engage in business practices to freeze out biosimilar competition and increase demand and prices for Humira in the United States.

Discussion

AbbVie’s internal documents confirmed that complex marketing strategies supporting Humira’s growth began in 2013, 2 years before the finalization of US biosimilar regulations.^{2,3} The House Oversight Committee’s majority staff reports uncover that other manufacturers adopted similar strategies, leveraging US regulatory policy to favor high prices of several pharmaceuticals.²

FIGURE. Factors That May Be Associated With Humira Revenue Between 2011 and 2020



Several bipartisan proposals address anticompetitive strategies in biologic markets. Senators Klobuchar and Grassley's Preserve Access to Affordable Generics and Biosimilars Act (S 1428) would make some Paragraph IV settlement agreements illegal, especially those in which cash payments were made to generic entrants as part of the agreement. Representatives Johnson and Issa's Affordable Prescriptions for Patients Through Improvements to Patent Litigation Act (HR 2884) would limit product hopping and abuse of the "patent dance" provision for biosimilars, which requires the intellectual property to be shared between biosimilar and reference biologic manufacturers. Representatives Maloney, Buck, and Cicilline's Affordable Prescriptions for Patients Through Promoting Competition Act (HR 2873) would amend the Federal Trade Commission Act to prohibit product hopping. Representatives Jeffries, Maloney, and Buck's Stop STALLING Act (HR 2883) would address "sham" citizen petitions. In the regulatory environment, Representative Maloney has requested that the Federal Trade Commission investigate AbbVie's Paragraph IV settlement agreements.

Policy makers have been introducing legislation to address competition in the prescription drug market for years, often reintroducing the same bills. The gridlock in Congress has prevented—and likely will continue to hinder—efforts to support biologic competition through legislation. Indeed, it is promising that some proposals have bipartisan sponsorship.

While Congress attempts to pass legislation, courts have had to take on antitrust issues in biologic markets. In a landmark ruling in 2020, Judge Manish S. Shah of the US District Court for the Northern District of Illinois dismissed complaints from the United Food and Commercial Workers' Local 1500 Welfare Fund that AbbVie's patent thickets and Paragraph IV settlement agreements violated the Sherman Antitrust Act, which differs from the decisions from the Supreme Court case *Federal Trade Commission v Actavis, Inc*, 570 US 136 (2013).⁵ This ruling is under appeal.⁶ The Federal Trade Commission submitted an amicus brief in support of neither party in the trial.⁷ The brief indicated that under the 2013 Actavis Supreme Court decision (which found that some Paragraph IV settlement agreements were anticompetitive and therefore unlawful), the legality of a Paragraph IV settlement turns on the presence of a large payment and reasons for the payment.⁸ The presence of a settlement payment and an agreement by biosimilars to delay their entry is not currently enough to determine the legality of a Paragraph IV settlement. Under Actavis, biosimilar manufacturers can settle patent litigation with reference biologic manufacturers if the payments reflect traditional settlement considerations, such as litigation cost avoidance for fair market value. Hence, the judge's decision on the appeal may hinge on specific contract details included in the Paragraph IV settlement agreements. If the appeal prevails, more Paragraph IV settlements could be considered anticompetitive and illegal in future cases. Court decisions such as in this appeal can build on the Actavis case decision supporting evaluations of Paragraph IV settlement agreements in determining if these settlements are truly anticompetitive.

Conclusions

AbbVie has spent years engaging in strategies to increase Humira revenues and protect the product from biosimilar competition. These strategies are not unique to AbbVie and shed light on pharmaceutical market dynamics that may be hindering a competitive market.

To ensure sufficient competition in biologic markets, policy makers will need to carefully review the House Oversight Committee's 2021 majority staff report on Humira pricing and develop bipartisan legislation to protect market competition. More broadly, efforts are needed to shape regulatory landscapes that promote competition while encouraging innovation. Until congressional lawmakers find agreement on the path forward, decision-making power lies in the courts. Policy reform and legal initiatives may help reduce anticompetitive behaviors by pharmaceutical manufacturers and increase access to competitive therapeutic options such as biosimilars. ■

Acknowledgments

The authors would like to acknowledge helpful comments on early versions of this manuscript by Gerard Anderson, PhD; Caleb Alexander, MD, MPH; Tom Moore; Jeromie Ballreich, PhD; Mariana Social, MD, PhD, MPP; and Antonio Trujillo, PhD, of the Johns Hopkins Bloomberg School of Public Health in Baltimore, MD.

Author Affiliations: Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health (JBG, ML), Baltimore, MD; SmartState Center for Medication Safety and Efficacy, University of South Carolina College of Pharmacy, and Department of Clinical Outcomes and Effectiveness, The Beckman Institute (CLB), Columbia, SC; City of Hope Comprehensive Cancer Center (CLB), Duarte, CA.

Source of Funding: Unrestricted grants from Arnold Ventures (JBG), the National Cancer Institute (1R01 CA102713) (CLB), and the Frank Martin Research Fund of the City of Hope Cancer Center (CLB).

Author Disclosures: Dr Gibbons reports receiving unrestricted grants from Arnold Ventures. Dr Bennett reports receiving unrestricted grant support from the City of Hope Cancer Center. Ms Laber reports no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (JBG, CLB); analysis and interpretation of data (ML, CLB); drafting of the manuscript (JBG, ML, CLB); critical revision of the manuscript for important intellectual content (JBG, ML); obtaining funding (JBG); and administrative, technical, or logistic support (ML).

Address Correspondence to: Jason B. Gibbons, PhD, Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe St, Baltimore, MD 21205. Email: jgibbo13@jhu.edu.

REFERENCES

- Dunleavy K. Humira rings up \$20.7 billion in 2021, but AbbVie still mum on post-biosimilar expectations. *Fierce Pharma*. February 2, 2022. Accessed February 25, 2022. <https://www.fiercepharma.com/pharma/humira-rings-up-20-7-billion-sales-but-abbvie-still-mum-a-projection-for-2023-when-it-faces>
- Drug pricing investigation: AbbVie—Humira and Imbruvica. US House of Representatives Committee on Oversight and Reform. May 2021. Accessed February 25, 2022. <https://web.archive.org/web/20221209115021/https://oversight.house.gov/sites/democrats.oversight.house.gov/files/Committee%20on%20Oversight%20and%20Reform%20-%20AbbVie%20Staff%20Report.pdf>
- Drug pricing investigation: majority staff report. US House of Representatives Committee on Oversight and Reform. December 2021. Accessed February 25, 2022. <https://web.archive.org/web/20221222175935/https://oversight.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf>
- Leading pharmaceutical brands in the United States in March 2021, by national TV ad spend. Statista. Accessed February 25, 2022. <https://www.statista.com/statistics/639356/tv-advertise-drugs-usa/>
- Shah MS. In re: Humira (adalimumab) antitrust litigation: memorandum opinion and order. US District Court for the Northern District of Illinois. June 8, 2020. Accessed February 25, 2022. <https://images.law.com/contrib/content/uploads/documents/398/55864/In-re-Humira-antitrust-litigation.Shah-order.pdf>
- UFWC Local 1500 Welfare Fund et al v AbbVie Inc*, 20-2402 (7th Cir 2020).
- Brief of amicus curiae the Federal Trade Commission in support of no party. Federal Trade Commission. October 13, 2020. Accessed February 25, 2022. https://www.ftc.gov/system/files/documents/amicus_briefs/ufwc-local-1500-welfare-fund-et-al-v-abbvie-inc-et-al/ufwc_local_1500_welfare_fund_amicus_brief.pdf
- Federal Trade Commission vs Actavis, Inc*, 570 US 136 (2013).

Visit ajmc.com/link/89315 to download PDF