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An Investigation of when the Antitrust Agencies are likely to challenge a Pay-for-Delay Settlement under *ACTAVIS*

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ABSTRACT

In *FTC v. Actavis*, the U.S. Supreme Court held that a large, unjustified reverse payment in a pay-for-delay settlement might be classed as anticompetitive. However, neither the courts nor academia have clearly defined what a "large and unjustified" reverse payment entails. Thus, it is difficult to predict when a given pay-for-delay settlement might be challenged by the antitrust agencies. To establish a better prediction, this paper used machine learning to develop two decision tree models based on numerical and categorical data. The former model considers the duration of the generic drug delay entering the market and the estimated reverse payment, while the latter regards the status of the generic entry and the scale of the estimated reverse payment. Using the results of the decision tree models, a payment should be deemed large and unjustified if the estimated reverse payments for pay-for-delay settlements based on generic entry status to delay the entry of generic drugs exceed USD $24 million (2021). Pharmaceutical companies can use the results of the decision trees to predict whether past or future pay-for-delay settlements will be classified as large and unjustified thereby lowering the risks of being challenged from antitrust agencies.

Keywords: Reverse Payment, Pay-for-delay settlement, Antitrust Agencies, Machine Learning, Decision Tree

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An Investigation of when the Antitrust Agencies are likely to challenge a Pay-for-Delay Settlement under ACTAVIS

INTRODUCTION

In the 2013 case *FTC v. Actavis,*[1] the U.S. Supreme Court made five key judgments about how lower courts should analyze pay-for-delay agreements[2] from an antitrust perspective.[3] First, pay-for-delay agreements between brand-name and generic manufacturers have the "potential for genuine adverse effects on competition."[4] Second, the adverse effects on competition may be justified because the compensation that the generic manufacturer receives could be greater than the avoided patent litigation costs and may also cover other services that the generic firm has promised, such as distributing or helping to develop a market for the patented item.[5] Third, the size of the payment may also reflect the brand-name company's market power because firms with significant market influence can charge higher than competitive prices.[6] Fourth, an unexplained large reverse payment normally suggests that the patentee has serious doubts about the patent's survival.[7] Furthermore, it is normally unnecessary to litigate a patent's validity to determine whether a pay-for-delay settlement is injurious to competition.[8] Fifth, the fact that a large, unjustified reverse payment risks violating antitrust laws does not prevent the litigants from settling a suit.[9] Thus, the purpose of the settlement plays a key role in its analysis. Courts should invalidate agreements that maintain and divide patent-generated monopoly profits between the brand-name and generic manufacturers without a sufficient justification.[10]

In *Actavis*, the justices used the terms "unexplained large reverse payment" and "large, unjustified reverse payment" to describe pay-for-delay agreements that might be anticompetitive.[11] However, they failed to clarify exactly how large such

1. FTC v. Actavis, Inc., 570 U.S. 136 (2013).

2. A pay-for-delay agreement is generally a form of patent dispute settlement where a pharmaceutical patent holder extends to a generic company some sort of value transfer, for instance direct monetary payment, distribution or licensing rights and/or other forms of considerations in return for which the generic company acknowledges the validity of the patent in dispute and undertakes to refrain from marketing a generic version of drugs which is equivalent to the originator drugs for a specified period of time at the end of the life of the patent. The consideration in return for the delay of the generic drug in above situation is also called reverse payment. Tay and Partners, *The Notorious "Pay-for-Delay" Agreement*, LEXOLOGY, https://www.lexology.com/library/detail.aspx?g=eacd6026-39c5-4c49-8b66-47ba05eedf8c (last visited November 1, 2021).

3. *Actavis, Inc.*, 113 U.S. at 141.

4. *Id.* at 153 (*citing* FTC v. Indiana Fed'n of Dentists, 476 U. S. 447, 460-61 (1986)).

5. *Id.* at 156.

6. *Id.* at 157.

7. *Id.*

8. *Id.*

9. *Id.* at 158.

10. *Id.*

11. *Id.* at 157-58.

payments are or how their size should be determined. Instead, they only laid down the factors to be considered when determining whether payments might be anticompetitive, such as the avoided litigation cost and other services that are included in the payment.[12] Thus, pharmaceutical companies have difficulty predicting whether their past and future pay-for-delay settlements might be challenged by the antitrust agencies.[13]

This paper aims to provide a clear, standardized method by which the antitrust agencies are likely to challenge a pay-for-delay settlement under *Actavis* by evaluating which sizes of reverse payments would be classified as large and unjustified and in which situations pharmaceutical manufacturers could significantly risk being challenged by antitrust agencies. In Part II, we explore how the lower courts, the Federal Trade Commission (FTC), and other scholars have dealt with and determined whether their research can provide any useful indicators for how to define large and unjustified payments. In Part III, we discuss our assumptions, data collected from different sources, and associated challenges. For this, we collate 162 available abbreviated new drug application (ANDA) patent litigation settlements and categorize them into numerical and categorical data. In Part IV, we use these two categories to develop decision trees while applying the Gini Index and Entropy criteria. In Part V, we address the implications of our results to answer our research question and make proposals for pharmaceutical manufacturers about how to use the results of our decision trees to avoid antitrust-associated risk when making pay-for-delay settlements. Part VI concludes our findings and acknowledges the limitations of this paper.

I. PRECEDENTS AFTER *ACTAVIS* AND LITERATURE DISCUSSIONS

As mentioned above, in *Actavis*, the justices failed to clarify exactly how large such payments are or how their size should be determined.[14] However, this has not stopped courts from applying language from *Actavis* to render their decisions.[15] According to our survey, from 2014 to 2019 (See Appendix), after *Actavis*, judges used two methods to analyze pay-for-delay settlements under *Actavis* guidelines.[16]

12. *Id.* at 159.

13. Valeria Bauman, *Pharma Pay-For-Delay Deals Called 'Cost of Doing Business'*, BLOOMBERG L. (Feb. 10, 2020, 5:30 A.M.), https://news.bloomberglaw.com/pharma-and-life-sciences/pharma-pay-for-delay-settlements-cost-of-doing-business.

14. FTC v. Actavis, Inc., 570 U.S. 136, 159 (2013).

15. *See e.g. In re* Zetia (Ezetimibe) Antitrust Litig., No. 2:18-md-2836, 2019 WL 1397228, at *12 (E.D. Va. Feb. 6, 2019) (*citing* Actavis, 113 U.S. at 157) (applying *Actavis* and reasoning that "'[a]n unexplained large reverse payment itself would normally suggest that the patentee has serious doubts about the patent's survival.' If so, then its objective may be 'to maintain supra-competitive prices to be shared among the patentee and the challenger.' Such 'large and unjustified' reverse payments raise antitrust concerns and subject the agreement to scrutiny for antitrust harms.").

16. *See infra* App'x pp. 34-35.

The first directly applies the language from *Actavis* to a given case.[17] That is, the courts have attempted to interpret the meaning of "large, unjustified reverse payment," with the majority interpreting it literally.[18] For instance, in *In re Loestrin 24 Fe Antitrust Litigation*[19], the judge required that the plaintiffs plead information sufficient "to estimate the value of the term, at least to the extent of determining whether it is 'large' and 'unjustified.'"[20] In the recent *In re Zetia (Ezetimibe) Antitrust Litigation*, the court explained that such large and unjustified reverse payments raise antitrust concerns and make their underlying agreements vulnerable to antitrust scrutiny.[21] The second method addresses the elements that plaintiffs must prove are present in a pay-for-delay agreement.[22] For instance, in *In re Cipro Cases I & II*[23], the court stated:

A third-party plaintiff challenging a reverse-payment patent settlement must show four elements: (a) the settlement includes a limit on the settling generic challenger's entry into the market; (b) the settlement includes cash or equivalent financial consideration flowing from the brand to the generic challenger; and the consideration exceeds (c) the value of goods and services other than any delay in market entry provided by the generic challenger to the brand, as well as (d) the brand's expected remaining litigation costs absent settlement.[24]

Although this approach has not been widely adopted by other courts, it represents a first step in attempting to resolve this complex issue. However, neither of these methods clearly defines the factors that make payments large and unjustified. For example, they fail to clarify whether all payments that are larger than future litigation costs are unjustified. Therefore, if several pay-for-delay settlements have payments that are larger than future litigation costs, pharmaceutical manufacturers can hardly predict whether those settlements are likely to be challenged by antitrust agencies.[25]

Furthermore, we also found that the FTC has not provided any guidelines to decide whether a payment in a pay-for-delay agreement can be classified as large

17. *See infra* App'x pp. 34-35.

18. *See infra* App'x pp. 34-35.

19. Rochester Drug Co-Operative, Inc. v. Warner Chilcott Co. (In re Loestrin 24 Fe Antitrust Litig.), 814 F.3d 538 (1st Cir. 2016).

20. *Id.* at 552 (quoting *In re* Actos End Payor Antitrust Litig., No. 13–CV–9244 (RA), 2015 WL 5610752, at *13 (S.D.N.Y. Sept. 22, 2015)).

21. *In re Zetia (Ezetimibe) Antitrust Litig., 400 F. Supp. 3d 418, 425 (E.D. Va. 2019) (citing FTC v. Actavis, Inc., 570 U.S. 136, 159 (2013)).*

22. *See infra* App'x pp. 34-35.

23. *In re* Cipro Cases I & II, 348 P.3d 865 (2015).

24. *Id.* at 865.

25. *See supra* text accompanying note 13.

and unjustified.[26] The FTC is able to access and publish data from settlements between brand-name and generic manufacturers because the 2003 Medicare Prescription Drug, Improvement, and Modernization Act requires manufacturers to report their patent litigation settlements to the FTC.[27] The FTC's 2016 report analyzing settlement data shows that 30 final settlements contained both explicit compensation from a brand-name manufacturer to a generic manufacturer and a restriction on the generic manufacturer's ability to market its products competitively against the brand-name manufacturer's products.[28] Most notably, 29 of these 30 agreements contained payments for avoided litigation from the brand-name manufacturer to the generic manufacturer of $250,000–$7,000,000, with the average payment standing at $2.85 million and two of the 29 payments totaling in excess of $7 million.[29]

These statistics show the range of reverse settlement payments from brand-name companies to generic companies. It is difficult for brand-name and generic manufacturers, however, to determine precisely where within this range payments become large and unjustified because, for example, a payment of $7 million may actually be small in relation to expected litigation costs. Thus, the statistics published by the FTC did not tell pharmaceutical manufactures the circumstances under which a pay-for-delay settlement might be challenged.[30]

As of the commentary after *Actavis*, Former FTC Commissioner Joshua D. Wright proposed to answer the central question of this paper regarding whether reverse payments greater than avoided litigation costs are large and unjustified.[31] Wright's answer addressed two approaches to this issue. One approach was proposed by Edlin et al. (2013) in their article titled *Activating Actavis*, which states that the amount of the reverse payment should be less than the avoided litigation costs, and that other considerations provided by the claimed infringer to the patentee can reflect the strength of a patent and can be understood as a payment for delaying

26. We found that the FTC only provides the basic statistics of settlements between the generic and the brand drug manufacturers.

27. Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. 108–173 § 1112, 117 Stat. 2461 (2003) (requiring that brand-name drug manufacturers, generic drug applicants, and biosimilar biological product applicants file certain agreements with the FTC and the Department of Justice within 10 business days of executing agreements.).

28. Bureau of Competition, *Agreements Filed with the Federal Trade Commission under the Medicare Prescription Drug, Improvement, and Modernization Act of 2003: Overview of Agreements Filed in FY 2016*, FTC, https://www.ftc.gov/system/files/documents/reports/agreements-filled-federal-trade-commission-under-medicare-prescription-drug-improvement/mma_report_fy2016.pdf(last visited Sep. 3, 2021).

29. *Id.*

30. *Id.*

31. *See* Joshua D. Wright, Comm'r, Fed. Trade Comm'n, Antitrust Analysis of Reverse Payment Settlements after Actavis: Three Questions and Proposed Answers—Remarks at the Antitrust Masters Course VII (Oct. 10, 2014) (transcript available on the Federal Trade Commission website).

entry.[32] The theory underlying this approach is based on the monopoly-to-duopoly model that assumes entry by a single generic manufacturer.[33] The brand-name manufacturer would lose profits when a generic manufacturer enters the market, and the avoided litigation costs are based on this monopoly-to-duopoly model.[34]

A different approach was proposed by Harris et al. (2014) in a response to *Activating Actavis* titled *Activating Actavis: A More Complete Story.* The authors argued that the avoided litigation costs do not reflect the benefits of settlements to consumers because settlements sometimes occur before patents expire.[35] As a result, incorporating avoided litigation costs into the determination of large and unjustified payments would reduce the number of settlements that benefit consumers.[36]

Ultimately, Wright seemed to favor the second approach, arguing that avoided litigation costs should not be included in the determination because the monopoly-to-duopoly model does not reflect the institutional reality that multiple manufacturers can enter a market after a patent is invalidated.[37] This is due to the fact that the generic manufacturer that successfully challenges a patent's validity would be granted the right to be the sole entrant for only 180 days, not for the remaining lifetime of the patent.[38] The greater the number of generic entrants, the smaller their profits.[39] By accounting for possible losses due to multiple entrants, settlements between brand-name and generic manufacturers would benefit consumers while also exceeding avoided litigation costs.[40]

Other scholars have also expressed their opinions regarding *Actavis.* For instance, in 2014, Herbert Hovenkamp discussed the relationship between patent validity and pay-for-delay settlements.[41] He claimed that the size of the payment should play a key role in determining whether it is large and unjustified, as it reflects the probability of the patent being invalidated, the value of the remaining lifetime of the patent, and the harm it may cause to the market because of the delay of the

32. Aaron Edlin, Scott Hemphill, Herbert Hovenkamp & Carl Shapiro, *Activating Actavis*, 28 ANTITRUST 16, 16 (2013).

33. Carl Shapiro, *Antitrust Limits to Patent Settlements*, 34 RAND J. ECON. 391, 399 (2003).

34. Murat Mungan, *Reverse Payments, Perverse Incentives*, 27 HARV. J.L. & TECH. 1, 5 (2013); Einer Elhauge & Alex Krueger, *Solving the Patent Settlement Puzzle*, 91 TEX. L. REV. 283, 298 (2012).

35. Barry C. Harris, Kevin M. Murphy, Robert D. Willig & Matthew B. Wright, *Activating Actavis*: *A More Complete Story*, 28 ANTITRUST 83, 83 (2014).

36. *Id.* at 88.

37. Wright, *supra* note 31, at 12.

38. *Id.* at 12-13.

39. *Id.* at 14.

40. *Id.*

41. Herbert Hovenkamp, *Anticompetitive Patent Settlements and the Supreme Court's Actavis Decision*, 15 MINN. J.L. SCI. & TECH. 3, 6 (2014).

generic entry.[42] Thus, patent validity may be one of several factors that affect the size of settlements.[43] Furthermore, Hovenkamp argued that pay-for-delay settlements are unrelated to patent validity, as they may also reflect the profit-sharing that would occur between brand-name and generic manufacturers during the 180-day exclusivity period granted to generic manufacturers who successfully sue to invalidate brand-name manufacturers' patents under the Hatch–Waxman Act.[44] Thus, Hovenkamp concluded that patent validity alone cannot determine whether a pay-for-delay agreement violates antitrust laws.[45]

Michael A. Carrier expounded on a means for determining whether a payment from a brand-name to a generic manufacturer constitutes an exclusion payment that would violate antitrust laws.[46] His method begins with an analysis of two elements to ascertain whether the payment is justified.[47] First, payments that do not exceed litigation costs are not classed as exclusion payments, as the brand-name manufacturer is expected to have paid these costs regardless of whether litigation occurred.[48] Second, payments can be made for services unrelated to the generic manufacturer's postponement of market entry.[49]

After the justification analysis, two more elements are analyzed to determine the exclusion payment.[50] First, whether the brand conveys to the generic a type of consideration unavailable as a direct consequence of winning the lawsuits is assessed.[51] Second, payments considered as a direct consequence are then analyzed to determine whether the generic manufacturer is excluded from the market due to the strength of the brand-name manufacturer's patent.[52] As valid patents provide the brand-name manufacturer a right to exclude, the payment due to the validity of the patents can be justified.[53] Nonetheless, Carrier argues that exclusions not due to the brand-name manufacturer's market power may violate antitrust laws because payments would rise beyond what a valid patent could justify.[54]

Instead of debating which payments would be considered large and unjustified under *Actavis*, several scholars have sought to predict the real-world effects of

42. *Id.* at 10-13.
43. *Id*. at 10.
44. *Id.* at 12.
45. *Id.* at 20-21.
46. Michael A. Carrier, *Payment after Actavis*, 100 IOWA L. REV. 7, 9 (2014).
47. *Id.* at 19.
48. *Id.*
49. *Id.* at 21-22.
50. *Id. at 26-27.*
51. *Id.* at 26.
52. *Id.* at 26.
53. Michael A. Carrier, *Payment after Actavis*, 100 IOWA L. REV. 7, 27 (2014).
54. *Id.* at 27-28.

Actavis.[55] For example, Allison Schmitt discussed how brand-name manufacturers have extended their exclusivity periods by using secondary patents for elements beyond the active compound itself.[56] However, these patents are easily invalidated by Hatch–Waxman litigation.[57] Thus, if secondary patents become the main focus of litigation for which the manufacturers settle, the application of the Hatch–Waxman Act might encounter obstacles.[58]

In 2016, Feldman and Frondorf analyzed how the brand-name and the generic manufacturers delay the release of generic drugs, suggesting that delays occur in three stages.[59] The first stage is when brand-name manufacturers simply pay generic manufacturers to delay their entry into the market.[60] The second stage is when brand-name and generic manufacturers engage in multiple side deals to conceal the value of settlement payments.[61] These side deals may take several forms. For instance, the settlements may feature an acceleration clause that allows the generic manufacturer to enter the market immediately if another generic manufacturer is also able to enter before the end of the 180-day exclusivity period.[62] Another type of deal contains a no-Authorized Generic clause that prevents the brand-name manufacturer from launching any authorized generic drugs in exchange for the generic manufacturer delaying its entry.[63] This clause allows the brand-name manufacturer to continue to sell its patented drug until the end of the 180-day exclusivity period.[64] The third stage involves a variety of techniques, one example of which is known as "product-hopping."[65] An example of product-hopping is when AstraZeneca made its original prescription drug Prilosec into an over-the-counter drug before introducing its newly patented prescription drug Nexium.[66] Before the patent expired, Prilosec had already become the best-selling drug in the U.S. market with over $6 billion in annual sales.[67] In 2013, 12

55. Allison A. Schmitt, *Competition Ahead? The Legal Landscape for Reverse Payment Settlements after* Federal Trade Commission v. Actavis, Inc., 29 BERKELEY TECH. L.J. 493, 493-44 (2014).

56. *Id.* at 503.

57. *Id.* at 532-33.

58. *Id.* at 533.

59. Robin Feldman & Evan Frondorf, *Drug Wars: A New Generation of Generic Pharmaceutical Delay*, 53 HARV. J. ON LEGIS. 499, 504-05 (2016).

60. *Id.* at 510.

61. *Id.* at 516.

62. *Id.* at 521.

63. *Id*. at 522.

64. *Id.*

65. *Id.* at 525.

66. Robin Feldman & Evan Frondorf, *Drug Wars: A New Generation of Generic Pharmaceutical Delay*, 53 HARV. J. ON LEGIS. 499, 527 (2016).

67. *Id.* at 529.

years after its launch, Nexium was the second best-selling drug in the U.S. market with just under $6 billion in annual sales.[68]

Overall, the literature shows that only a small number of courts and scholars have attempted to define precisely what constitutes large and unjustified payments.[69] However, under *Actavis*, large and unjustified payments are the key factor in determining whether a pay-for-delay settlement might be challenged by the antitrust agencies, so the lingering confusion over the issue makes it difficult for pharmaceutical manufacturers to properly evaluate the risk of being challenged when making pay-for-delay settlements.[70] Thus, this paper endeavors to define the types of payments that qualify as large and unjustified for antitrust agencies and how pharmaceutical manufacturers should manage the risk that pay-for-delay settlements will be challenged by the antitrust authorities.

II. DATA

A. Assumptions

To achieve our research goals, we first created a dataset for decision tree models. According to the guidelines in *Actavis* and the literature above, the four elements correlated to whether a settlement payment is large and unjustified are the date of the settlement, the expiration date of the last qualifying patent, whether generic manufacturers have already entered the market, and the size of the settlement payment.[71]

Due to the difficulty in collecting data, we made four assumptions to simplify the data-collection process. First, we took the date of the settlement as the termination date of the ANDA patent litigation. Second, we assumed that the only factor preventing generic manufacturers from entering the market was the patent expiration date and that pediatric exclusivity[72] would not impact the generic entry. Third, we assumed that all the pay-for-delay settlements have cash payments and that the amount of the payments were determined by the judges or were determined by using the estimated reverse payment ratio based on the function of ANDA Paragraph IV (to accelerate the entry of generic manufacturers into the

68. *AstraZeneca Holds off Rivals as Drug Patent Dies*, USA TODAY (Oct. 5, 2001, 1:38 PM), http://usatoday30.usatoday.com/money/general/2001-10-05-prilosec.htm.

69. *See* Michael A. Carrier, *Payment After Actavis*, 100 IOWA L. REV., 7, 7 (2014). Specifically, we only found that Professor Carrier discussed the meaning of the large and unjustified payment under *Actavis*. *Id.*

70. FTC v. Actavis, Inc., 570 U.S. 136, 158-59 (2013).

71. *Id* at 170-71.

72. *The Pediatric Exclusivity Provision*, FDA, https://www.fda.gov/science-research/pediatrics/pediatric-exclusivity-provision (last updated Mar. 22, 2018) ("In 1997, as part of the Food and Drug Administration Modernization Act (FDAMA) (Pub. L. 105-115), Congress enacted a new law that provides marketing incentives to manufacturers who conduct studies of drugs in children. This law, which provides six months exclusivity in return for conducting pediatric studies, is commonly known as the pediatric exclusivity provision.").

market). In *Actavis*, the justices noted that one of the reasons why brand-name manufacturers make reverse payments is that they believe that they might lose the patent validity suit, thus accelerating the entry of the generic.[73] Without ANDA Paragraph IV, generic manufacturers would have to wait until relevant patents expire before entering the market.[74] Settlements between manufacturers seem to diminish the function of ANDA Paragraph IV. Therefore, we assumed that estimated reverse payments were equal to the average reverse payment divided by the decrease in U.S. brand-name manufacturer investment spending on drugs due to patent expiration. In 2016, [75] the former was $2.85 million, and the latter was $1.4 billion,[76] yielding 0.203 percent. This ratio should be different every year, but the FTC did not disclose the mean annual reverse payment until the *2016 MMA Report* was published in 2019.[77] At the time of writing, it remains impossible to calculate a ratio for each year of analysis, so we have assumed that it was constant between 2014 and 2020.

B. Data Collection

Based on the assumptions above, we built our dataset from five types of data. The first was ANDA patent litigation settlements made between January 1, 2014, and August 31, 2020. Some settlements were challenged by the antitrust agencies, and others were not. This data was found via the JD Supra website[78] (which is targeted at business executives and in-house counsel), the Robins Kaplan LLP law firm website,[79] and a Westlaw database.

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73. *Actavis*, 570 U.S. at 157-58; *see supra* note 2.

74. *Patent Certifications and Suitability Petitions*, FDA https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions (last updated Nov. 2, 2021).

75. *Overview of Agreements Filed in FY 2016, A Report by the Bureau of Competition*, FTC (May 2019), https://www.ftc.gov/system/files/documents/reports/agreements-filled-federal-trade-commission-under-medicare-prescription-drug-improvement/mma_report_fy2016.pdf (When we wrote this paper in the fall of 2020, the latest MMA report was released in May 2019, which contained the results of settlements from FY 2016, which I used to calculate the ratio); *see supra* note 28.

76. Matej Mikulic, *Projected decrease in brand drug spending due to patent loss in the U.S. 2014-2024*, STATISTA (Jan. 6, 2021), https://www.statista.com/statistics/886733/decrease-in-drug-spending-due-to-loss-of-exclusivity-us/.

77. *Overview of Agreements Filed in FY 2016, A Report by the Bureau of Competition*, FTC (May 2019), https://www.ftc.gov/system/files/documents/reports/agreements-filled-federal-trade-commission-under-medicare-prescription-drug-improvement/mma_report_fy2016.pdf.

78. *See* Jeffrey Alan Hovden, Oren Langer, Kelsey McElveen & Christopher Pinahs, *ANDA Litigations Settlements – Spring 2020*, JDSupra (May 3, 2020), https://www.jdsupra.com/legalnews/anda-litigation-settlements-spring-2020-73758/ (providing a list of ANDA patent settlements that occurred in spring 2020).

79. *See ANDA Litigation Settlements Winter 2019*, Robins Kaplan LLP (2019), https://www.robinskaplan.com/resources/legal-updates/generically-speaking-hatch-waxman-bulletin/2019/generically-speaking-winter-2019/anda-litigation-settlements (providing the ANDA patent settlements that occurred in the winter of 2019).

The second data set was drawn from a database compiled by the FDA on Paragraph IV Patent Certifications made up to August 31, 2020. The database contains the drug name, dosage form, strength, NDA, date of submission, number of ANDAs submitted, 180-day status, 180-day decision posting date, date of first applicant approval, date of first commercial marketing, and expiration date of the last qualifying patent.[80] We collected the date of first commercial marketing and the expiration date of the last qualifying patent that involved the ANDA patent litigation settlements.

The third data type concerned the availability of generic drug-related ANDA patent litigation settlements. This data divulged that first-time generics are the first generic versions of marketed brand-name drug products to be approved by the FDA. The data was sourced via *Drugs.com*, which is the largest, most frequently visited independent medicine information website in the world.[81]

The fourth source was 10-K reports filed with the Securities and Exchange Commission by brand-name and generic manufacturers involved in the ANDA patent litigation settlements mentioned above. The 10-K reports record the amount of revenue a company earns for a particular drug in a given year in the U.S. market.[82] This data can be used to estimate the reverse payment for a pay-for-delay settlement.

The fifth data source was the revenue generated by a drug in a given year in the United States. This information was drawn from various sources, such as Statista and FiercePharma.

C. Limitations and Data Selection

Before introducing the decision tree analysis, it is necessary to describe how the data was selected and discuss any limitations related to this data. One of the data sources used in this work was the ANDA patent litigation settlements from January 1, 2014 to August 31, 2020. The greatest challenge with this data was finding the specific amount of revenue generated by a particular drug each year in the U.S. market. This data can be difficult to find because drug manufacturers may not want to disclose the individual financial performance of each of their products. Consequently, they sometimes combine their financial results and report global

80. *See Patent Certifications and Suitability Petitions*, FDA (Sept. 22, 2021), https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions (providing the latest certifications).

81. *See Generic Drugs - Availability and Patent Status*, Drugs.com, https://www.drugs.com/availability/ (providing a list of generic drugs and associated relevant data) (last visited Nov. 2, 2021).

82. *See* Merck & Co., Inc., Annual Report (Form 10-K), at 121 (Dec. 31, 2019), https://www.annualreports.com/HostedData/AnnualReportArchive/m/NYSE_MRK_2019.pdf, (providing Merck & Co., Inc.'s revenue streams for each of its drugs for FY 2019).

figures instead. Therefore, we had to delete settlements from our dataset when we could not find the amount of individual revenue generated in the U.S. market.

Settlements that included non-cash payments were also deleted.[83] In Feldman and Frondorf's paper, the authors demonstrated the importance of non-cash payments to pay-for-delay settlements. However, since it is difficult to evaluate the value of non-cash payments, settlements containing them were not included in our dataset. Moreover, settlements were deleted from the dataset if their core issue was not related to reverse payments, such as those concerned with patent on-sale prohibitions or product-hopping issues. Finally, settlements for drugs that were withdrawn from the market by the FDA after the settlement date were also removed from the dataset.[84]

The final dataset contained 162 ANDA patent litigation settlements, of which 13 were adjudicated by federal judges, and 149 were not challenged by antitrust agencies.

D. Data Categorization

Before running the decision trees, we first categorized the dataset. We established one dependent variable and two independent variables. The dependent variable was whether the settlement was being challenged by an antitrust agency. Thus, settlements that were being challenged were coded as *Y*, and those that were not being challenged were coded as *N*.

For the independent variable, the decision trees were run for two versions of the dataset. The first version contained only numerical data. The first independent variable was the duration between the date of settlement and the patent expiration date for each of the drugs for which settlements were reached, or the period between the date of settlement and a generic manufacturer's entry into the market. These durations were called years of delay (YoD). The YoD would be negative if a generic manufacturer entered the market before the date of settlement but would otherwise be positive. The second independent variable was the estimated reverse payment for each settlement calculated using the estimated reverse payment ratio mentioned above. These were denoted as Payments.

Another version of the dataset contained categorical data. The first independent variable was duration, which was coded according to when the generic

83. *See In re* Loestrin 24 Fe Antitrust Litig., 814 F.3d 538 (2016) (depicting an instance where Actavis Pharma, Inc. reached non-cash reverse payments).

84. *See FDA Requests the Withdrawal of the Weight-loss Drug Belviq, Belviq XR (lorcaserin) From the Market*, FDA (Feb. 19, 2020), https://www.fda.gov/drugs/fda-drug-safety-podcasts/fda-requests-withdrawal-weight-loss-drug-belviq-belviq-xr-lorcaserin-market (demonstrating that the FDA requested the withdrawal of the weight-loss drugs Belviq and Belviq XR (lorcaserin) from the market on February 13, 2020); *see supra* note 78 (referencing the ANDA litigation settlement of *Arena Pharms., Inc., v. Teva Pharms. USA, Inc.*).

manufacturer entered the market. Table 1 below illustrates the categorizations and their coding.

Table 1. Coding according to when the generic manufacturer entered the market

Categorizations	**Coding**
Settlements for drugs for which the generic manufacturer entered the market before the patent expired.	E
The generic manufacturer entered the market before the settlement date.	ES
The generic manufacturer entered the market on the date when the patent expired.	P
The generic drug had been approved by the FDA by the date of settlement, but the generic manufacturer could not enter the market because the relevant patents had not expired.	A
No therapeutically equivalent generic drug was available on the date of settlement.	N

The second independent variable was obtained by categorizing estimated payments into three groups by comparing them to the average patent litigation costs in the pharmaceutical industry. We took the figures from Carrier's paper, which showed that the range of Hatch–Waxman litigation costs was $2.65–$6 million.[85] We set $2 million as the threshold for the comparison with the estimated reverse payment and denoted "Payment Category" as the estimated payment category in the dataset. Estimated reverse payments greater than $2 million were coded as *L* for "large," those that were less than $2 million were coded as *S* for "small," and those for which the generic manufacturer entered the market before

85. Carrier, *supra* note 69, at 20.

the relevant patent expired were coded as *I* for "impossible" because no reverse payment could occur in such a situation.

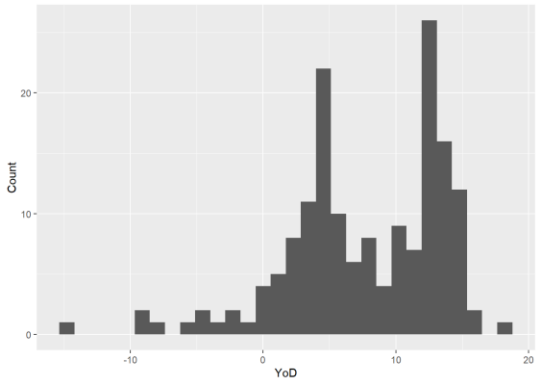
E. Description of the Data and Preliminary Observations

The 162 ANDA patent litigation settlements were all quantified and categorized with the same dependent variable. Table 2 and Figures 1 and 2 summarize the numerical data. If all the generic manufacturers had been successful in their patent invalidation suits, over half the generic drugs would have been delayed for at least eight years before the last qualifying patent expired. The most frequent delays were five years (23 settlements) and thirteen years (26 settlements).

Table 2. Numerical data summary

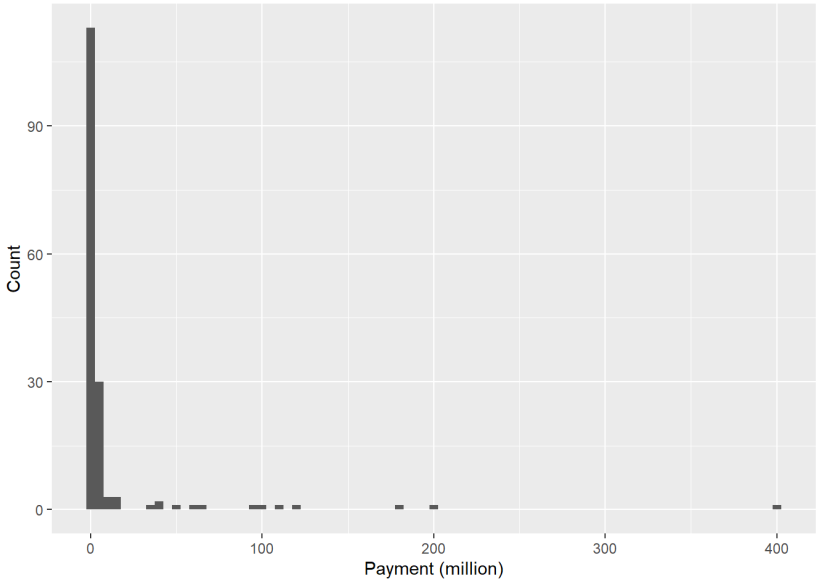
	YoD	**Estimated Payment ($)**
Minimum	−15	0
1st quartile	4	188,282
Median	8	1,032,255
Mean	7.631	10,735,946
3rd quartile	13	3,048,248
Maximum	18	398,100,000

Figure 1. Possible YoD



If all the brand-name manufacturers made reverse payments after they had settled, more than half of the estimated reverse payments would be approximately $1 million, which is less than the average related patent litigation cost. Thus, although more than half of the generic drugs may have been delayed due to settlements, the companies would have been justified in settling because the reverse payments were lower than the litigation costs.

Figure 2. Estimated reverse payments



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Two major findings emerged from the categorical data (Table 3). First, for almost half of the settlements, no therapeutically equivalent generic drug was available on the settlement date. Thus, even if the patents had been invalidated, consumers would still not have had access to a generic drug.

Second, 92% of settlements that were challenged by antitrust agencies had early generic manufacturer entry into the market. This result indicates that antitrust agencies may not be overly concerned about the status of generic manufacturer entry into the market when investigating pay-for-delay settlements.

Table 3. Generic manufacturer entry status

Decision	*Duration*					***Total***
	A	E	ES	N	P	
N	50 33.6 %	9 6 %	11 7.4 %	79 53 %	0 0 %	149 100 %
Y	0 0 %	12 92.3 %	0 0 %	0 0 %	1 7.7 %	13 100 %
Total	50 30.9 %	21 13 %	11 6.8 %	79 48.8 %	1 0.6 %	162 100 %

Finally, more than half of the actual or estimated reverse payments were smaller than the average related patent litigation costs. Therefore, these settlements could have justifiably been made to avoid being challenged (Table 4).

Table 4. Reverse payment amount compared to litigation costs

Decision	*Payment category*			***Total***
	I	L	S	
N	11 7.4 %	46 30.9 %	92 61.7 %	149 100 %
Y	0 0 %	12 92.3 %	1 7.7 %	13 100 %
Total	11 6.8 %	58 35.8 %	93 57.4 %	162 100 %

III. DECISION TREE ANALYSIS AND RESULTS

A. Decision Tree Analysis

Decision trees are a type of predictive model that utilizes observations to make conclusions about the target value of a process. In the tree structure, "leaves" represent classifications (also known as "labels"), non-leaf "nodes" represent features, and "branches" represent conjunctions of features that lead to classifications.[86] We used the decision tree method to determine actions that antirust agencies might take to scrutinize pay-for-delay settlements. Moreover, pharmaceutical manufacturers can also use the decision tree method proposed in this study to predict which pay-for-delay settlements will be challenged.

86. Khaled Alsabti, Sanjay Ranka & Vineet Singh, *CLOUDS: A Decision Tree Classifier for Large Datasets*, (Aug. 1998), https://www.aaai.org/Papers/KDD/1998/KDD98-001.pdf.

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B. Results

After developing the datasets, we programmed our model in R using both versions of the datasets and by applying the Gini Index[87] and entropy criteria.[88] The results of the model generally included two parts: the decision tree and its performances. The decision tree is a visual representation of the classification table. The performance of the model includes three measures: classification table, accuracy and hit rate. The classification table illustrates the detailed results of the decision tree and is used to determine whether the algorithm made any categorization errors. The accuracy and the hit rate are correlated. While the accuracy shows the results of the correct categorization of both N-type and Y-type settlements, the hit rate specifically looks at the accuracy of the categorization of Y-type settlements in the classification table. The hit rate number is important because it tells us the accuracy of this model being used for evaluating when a pay-for-delay settlement might be challenged by the antitrust agencies. Finally, because the results under Gini Index and entropy criteria are similar, we chose the results under Gini index to be illustrated in this paper.

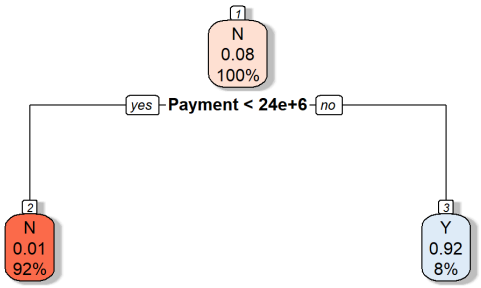
Version 1: Numerical Analysis

Two major findings emerged from our analysis (see Figure 3). First, settlements with estimated reverse payments of less than $24 million will likely not be challenged by antitrust agencies in the future. Second, YoD did not affect antitrust agencies' decisions regarding whether to challenge a settlement.

87. *See* Laura E. Raileanu & Killian Stoffel, *Theoretical Comparison between the Gini Index and Information Gain Criteria* (2004), https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.57.9764&rep=rep1&type=pdf (providing a more in-depth introduction).

88. *See* CLAUDE SAMMUT & GEOFFREY I. WEBB, ENCYCLOPEDIA OF MACHINE LEARNING AND DATA MINING, (Claude Sammut & Geoffrey I. Webb eds., 2d ed. 2017) (providing an introduction to entropy). An introduction to entropy is addressed in Fürnkranz J. *Decision Tree. In: Sammut C., Webb G.I. (eds) Encyclopedia of Machine Learning*. Springer, Boston, MA (2011). Available at https://doi.org/10.1007/978-0-387-30164-8_204.

Figure 3. Numerical data decision tree



As to the performance in Table 5, the decision tree correctly categorized almost all N- and Y-type settlements. Only 1 N-type settlement and 1 Y-type settlement were wrongfully categorized. Moreover, by calculating the accuracy of the decision tree, we got 0.987. This number suggests that, by having $24 million as the standard to categorize the numerical data, the accuracy of the categorization is 98%. Finally, the hit rate of the Version 1 model is 0.923. This number suggests that, if we use $24 million as a standard for our numerical data to categorize whether they are exactly Y-type settlements, the accuracy of the categorization is 92.3%.

Table 5. Version 1 classification table

Decision	*Prediction* N	Y	***Total***
N	148 99.3 %	1 0.7 %	149 100 %
Y	1 7.7 %	12 92.3 %	13 100 %
Total	149 92 %	13 8 %	162 100 %

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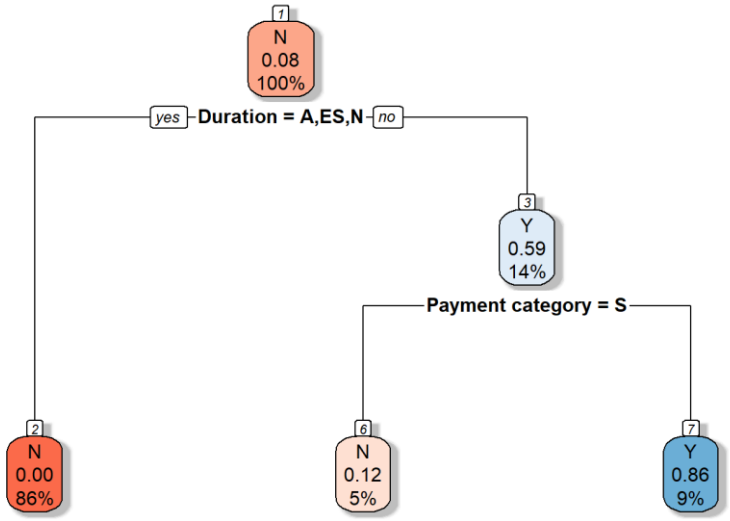
Version 2: Categorical Analysis

Version 2 also produced two major findings (see Figure 4). First, antitrust agencies did not challenge A-, ES-, and N-type settlements. For E- and P-type settlements, S-type reverse payments were not challenged, but L-type payments were. Second, no predictions were made regarding the I-type settlements because none of them fell into the Y category (Table 4).

Figure 4. Categorical data decision tree



In terms of the performance, Table 6 reveals that Version 2 of the decision tree also correctly categorized almost all of the N- and Y-type settlements. Only 2 N-type

settlements and 1 Y-type settlement were erroneously categorized. By calculating the accuracy of the decision tree, we got 0.981. This number suggests that by classifying the categorical data with two sequential thresholds—whether the generic manufacturer enters the market with A-, ES-, and N-type settlements, and whether the amount of reverse payment in E- and P-type settlements are less than $2 million in litigation costs—the accuracy of the categorization is 98%. Finally, the hit rate of the Version 2 model is also 0.923. This number reveals that, if we use those two sequential thresholds as a standard for our categorical data to categorize whether they are exactly Y-type settlements, the accuracy of the categorization is 92.3%.

Table 6. Version 2 classification table

Decision	*Prediction*		***Total***
	N	Y	
N	147 98.7 %	2 1.3 %	149 100 %
Y	1 7.7 %	12 92.3 %	13 100 %
Total	148 91.4 %	14 8.6 %	162 100 %

C. Implications And Proposal

In this section, we answer our research question of when antitrust agencies will challenge a pay-for-delay settlement under *Actavis* and address a proposal for pharmaceutical manufacturers to avoid being challenged when making pay-for-delay settlements.

A. Pay-for-delay settlements with payments of more than $24 million are likely to be challenged, even if the generic manufacturers enter the market before the last qualifying patent expires.

Since the hit rate of Versions 1 and 2 decision trees are the same, we can summarize the findings from those two versions of the decision trees. Version 1 decision tree showed that payments greater than $24 million may have antitrust implications. Moreover, Version 2 showed how to use the status of a generic

manufacturer's entry into the market to classify a payment as unjustified. The payments in settlements in which the status of the generic manufacturer's entry into the market are E- and P-types may still be seen as unjustified. Combined with the points made in the preceding discussion, this value can be used as a threshold for determining whether further antitrust scrutiny is warranted. Thus, payments greater than $24 million for settlements with generic manufacturer market entry statuses that are E- and P-types may be considered large and unjustified and can therefore be challenged by antitrust agencies.

B. A proposal to pharmaceutical manufacturers

The results of the Version 1 and Version 2 decision tree analyses have implications for pharmaceutical companies that have settled or will settle patent litigation suits.

The Version 1 decision tree result indicates that pay-for-delay settlement payments that are less than $24 million are less likely to attract antitrust scrutiny than payments of more than $24 million. Therefore, manufacturers should be wary of making payments of more than $24 million.

Manufacturers should also examine the generic manufacturer market entry status and payment amount to determine what type of settlement would best help them avoid antitrust scrutiny. Specifically, pay-for-delay settlements worth less than $24 million are less likely to attract antitrust scrutiny if they meet any of the following criteria: the generic manufacturer enters the market before the date of the settlement, or the generic drug has been approved by the FDA, but its manufacturer cannot enter the market because relevant patents have not expired, or there is no therapeutically equivalent generic drug available on the date of settlement.

IV.CONCLUSION AND LIMITATIONS OF THIS PAPER

This paper uses two decision tree models to clarify when the antitrust agencies might challenge a given pay-for-delay settlement under *Actavis*. Version 1 indicated that antitrust agencies would be more likely to investigate payments of more than $24 million. Version 2 addressed how the status of generic manufacturer entry into the market affects the probability of a settlement attracting antitrust scrutiny. The results of both decision tree analyses can be used by pharmaceutical manufacturers to determine whether they can settle a pay-for-delay without the risk of being investigated by the antitrust agencies.

Although this paper can help pharmaceutical manufacturers evaluate the risks of being challenged for pay-for-delay settlements, we acknowledge that this study has several limitations. First, because there is no database of pay-for-delay settlements, and only a few settlements were challenged by antitrust agencies, the

amount of the data we collected is limited. We obtained only 162 available data for conducting the decision tree analysis. Thus, if we can collect more data of pay-for-delay settlements in the future, the results of the decision tree analysis could be optimized and tested. Second, the details of the pay-for-delay settlements will never be disclosed, unless they are litigated in the federal courts. Due to this limitation of disclosure, we can only assume that all N-type settlements in our dataset have cash payments in their settlements, even if some of them may in fact have no-cash payment. Third, since there is no open-free database of litigation costs for ANDA patent litigations, we can adopt only historical data from literature to compare with the estimated reverse payment in our dataset.

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APPENDIX

Table 1: Federal Courts of Appeal cases related to pay-for-delay agreements (Citations Omitted)

List of Case Names and Years	**Framework of analysis**
King Drug Co. of Florence, Inc. v. Smithkline Beecham Corp. (2015)	The Actavis's five lessons and rule-of-reason analysis.
In re Loestrin 24 Fe Antitrust Litigation. (2016)	The Actavis's five lessons and rule-of-reason analysis.
In re Wellbutrin XL Antitrust Litigation Indirect Purchaser Class (2017)	The Actavis's five lessons and rule-of-reason analysis.
In re Lipitor Antitrust Litigation. (2017)	The Actavis's five lessons and rule-of-reason analysis.

Table 2: District and state-level cases related to pay-for-delay agreements (Citation Omitted)

List of Case Name and Year	**Framework of analysis**
United Food & Commercial Workers Local 1776 v. Teikoku Pharma USA, Inc. (N.D. Cal. 2014)	The Actavis's five lessons and rule-of-reason analysis.
FTC v. Cephalon, Inc. (E.D. Pa. 2014)	The Actavis's five lessons and rule-of-reason analysis.
Time Ins. Co. v. Astrazeneca AB (E.D. Pa. 2014)	The Actavis's five lessons and rule-of-reason analysis.
F.T.C. v. AbbVie Inc. (E.D. Pa. 2015)	The Actavis's five lessons and rule-of-reason analysis.
In re Aggrenox Antitrust Litigation (D. Conn. 2015)	The Actavis's five lessons and rule-of-reason analysis.
In re Cipro Cases I & II (Cal. 2015)	Addressed the elements that plaintiffs must prove are present in a pay-for-delay agreement.
In re Solodyn (Minocycline Hydrochloride) Antitrust Litigation (D. Mass. 2015)	The Actavis's five lessons and rule-of-reason analysis.
In re K-Dur Antitrust Litigation (D.N.J. 2016)	Addressed the elements that plaintiffs must prove are present in a pay-for-delay agreement.
In re Asacol Antitrust Litigation (D. Mass. 2017)	The Actavis's five lessons and rule-of-reason analysis
In re Namenda Direct Purchaser Antitrust Litigation (S.D.N.Y. 2017)	The Actavis's five lessons and rule-of-reason analysis
Picone v. Shire PLC (D. Mass. 2017)	The Actavis's five lessons and rule-of-reason analysis
In re Zetia (Ezetimibe) Antitrust Litigation (E.D. Va. 2019)	The Actavis's five lessons and rule-of-reason analysis
In the Matter of Impax Laboratories, Inc. (F.T.C. 2018)	The Actavis's five lessons and rule-of-reason analysis

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