Continuing trends in U.S. brand-name and generic drug competition

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\section*{ABSTRACT}

\textbf{Objective}: To provide updated evidence in a series of analyses of U.S. trends over the past two decades in key financial metrics for branded drugs: market exclusivity periods (MEPs), the time between launch and first generic entry for new molecular entities (NMEs); the probability, timing and number of patent challenges under Paragraph IV of the Hatch-Waxman Act; and the intensity of generic penetration.

\textbf{Methods}: As previously, we used IQVIA National Sales Perspectives U.S. data to calculate MEPs for the 356 NMEs experiencing initial generic entry from 1995 through 2019, the number of generic competitors for twelve months afterward (by prior sales level), and generic shares. We calculated the probability, timing and number of Paragraph IV challengers using Abbreviated New Drug Application (ANDA) approval letters, the FDA website, public information searches, and ParagraphFour.com.

\textbf{Results}: For NMEs experiencing initial generic entry in 2017–19, the MEP was 13.0 years for drugs with sales greater than $250 million in 2008 dollars the year before generic entry (NMEs>$250 million), 14.1 years overall. One year later, brands’ average unit share was 18% for NMEs>$250 million, 23% overall. Ninety-three percent of NMEs>$250 million experiencing initial generic entry faced at least one Paragraph IV challenge (2019, three-year rolling average), an average of 6.0 years after brand launch (81% and 6.3 years for all NMEs). NMEs faced an average of 6.8 and 8.9 Paragraph IV challengers per NME, for all and NMEs>$250 million, respectively (2017–19 figures).

\textbf{Limitations}: All analyses were restricted to NMEs experiencing generic entry.

\textbf{Conclusion}: The average 2017–19 MEP of 13.0 years for NMEs>$250 million has changed relatively little over the past decade and remains lower than for all NMEs (14.1 years). Paragraph IV challenges are more frequent and occur earlier for NMEs>$250 million. Generic share erosion remains high for both NME types.

\section*{Introduction}

Since the passage in 1984 of the Hatch–Waxman Act (formally, the Drug Price Competition and Patent Term Restoration Act), U.S. pharmaceutical competition has continued to evolve, with increases in rates of both generic drug penetration and patent litigation over the past two decades. The Hatch-Waxman Act increased generic drug competition for small-molecule drugs, while also creating incentives for continued medical innovation and new drug development. Patent challenges by generic drug manufacturers have become commonplace, and brand-name drugs often experience rapid sales decline following generic drug market entry. As a result, new brand-name drugs typically rely on U.S. sales during a market exclusivity period (MEP), or the time between the market launch of a brand-name drug and the market launch of its first generic, to generate profits and fund future investment.

The Hatch-Waxman Act includes a number of provisions designed to facilitate approval by the Food and Drug Administration (FDA) of generic drugs intended for sale in the U.S., thereby encouraging generic drug entry. Among them, the law created an Abbreviated New Drug Application (ANDA) generic drug approval process that substantially shortened the time and reduced the cost associated with a generic drug FDA marketing application. Before the law’s passage, original safety and efficacy data were required for FDA market approval of generic drugs, meaning generic drug manufacturers were faced with the cost of repeating many of the corresponding brand-name drug manufacturers’ clinical trials. Under the new streamlined ANDA process, generic manufacturers only had to show bioequivalence to the corresponding brand-name reference product (i.e. that their product has the same active ingredient, labeled strength, dosage form, and route of administration). Generic manufacturers are also protected by a research exemption “safe harbor” from patent infringement lawsuits for the bioequivalence studies they must conduct to gain FDA marketing approval. This provision allows generic manufacturers to begin developing their generic counterparts to brand-name...
drugs prior to patent expiration without running afoul of
drug patent law, thereby accelerating generic drug market launch.

The Hatch–Waxman Act also created economic incentives for
generic manufacturers to file challenges to brand-name
drugs’ patents prior to expiration. Under a so-called
“Paragraph IV challenge”, a generic manufacturer filing an
ANDA notifies the FDA either: it claims its generic drug does
not infringe a listed patent of the corresponding brand-name
drug; or claims that the patent is not valid. If within forty-
five days of being notified a Paragraph IV ANDA has been
filed, the brand-name drug manufacturer sues the generic
drug company for patent infringement, the FDA may
approve the ANDA only after such time as the generic
company prevails in court or through settlement, or until after
the expiration of a thirty-month stay, whichever event comes
first. There is an additional incentive for generic manufac-
turers to challenge patents, as the first to file a successful
Paragraph IV challenge, receiving FDA final approval for its
application and earning the right to enter the market prior
to patent expiration, receives a valuable 180-day period of
generic drug marketing exclusivity. During these 180 days, its
generic drug is the only ANDA-approved generic version of
the branded drug that is allowed on the market, allowing it
to charge higher prices and realize higher sales and profits
than it would when additional competing generic drugs
launch. More than one generic manufacturer can earn 180-
day exclusivity for a given drug, as challenges are made at
the dosage form or strength level (e.g. the 15-milligram
strength oral tablet), and more than one generic manufac-
turer can share the first-to-file status, as it is determined by
the filing date. The 180-day exclusivity benefit earned applies
only to the relevant dosage form or strength (i.e. where the
manufacturer was the first-to-file).

The 180-day period of generic drug marketing exclusivity
generally is a critical profitability consideration for a generic
manufacturer. Generic unit sales during this period are made
by a single or just a few manufacturers (the one or few first-
filling generic drug manufacturers, and possibly an authorized
generic manufacturer), and generic drugs experience a rap-
idly increasing share of the total units sold. In addition, dur-
ing this period, generic manufacturers may set prices only
modestly below the branded drug’s price. A high share of
total units sold, at relatively higher prices than expected fol-
lowing the entry of additional generic drug manufacturers,
means there are strong incentives to be the first, or among
the first, to file a Paragraph IV challenge.

In addition to these provisions intended to encourage
generic drug competition, the law also created innovation
incentives for brand-name drug manufacturers. The patent
term restoration provision allows a brand-drug manufac-
turer to select a single patent on a drug and to extend it by up
to five years, in order to compensate it for the part of the time
spent conducting clinical trials in human subjects for the
drug and for the time the New Drug Application (NDA) was
being reviewed by the FDA. The patent selected can be
extended by no more than five years, regardless of the time
spent in clinical trials and under FDA review, and the remain-
ing patent term after FDA approval, cannot exceed 14 years,
including the extension. Innovative brand-name drugs are
also subject to so-called “data exclusivity.” That provision
prohibits the FDA from accepting a generic drug application
for review that relies on a reference branded drug’s data on
safety and efficacy for five years after the approval of the
branded drug (unless there is a Paragraph IV challenge when
the period is four years). Data exclusivity runs concurrently
with patent protection. In the case of a patent challenge,
FDA generic approval is stayed by up to 30 months to allow
courts to resolve patent challenges. Some generics may opt
to enter “at-risk” of later damages if district court litigation is
still ongoing after 30 months and the court later finds
against them in the litigation.

Under the Hatch–Waxman Act framework, therefore, the
MEP for new brand-name drugs reflects the interaction of a
number of factors, including provisions aimed at facilitating
erial generic entry, other provisions aimed at maintaining
incentives for innovation, and individual commer-
cial decisions.

Following the passage of the Hatch–Waxman Act, the use
of generic drugs has increased steadily, with generic prod-
ucts’ share of total prescriptions in the U.S. increasing from
36 percent in 1994 to 90 percent in 2019. Reasons for the
increase include the broad adoption by payers of plan provi-
sions that encourage generic drug use, including tiered for-
mularies that have lower patient out-of-pocket costs for
generic drugs than for brand-name drugs, step therapy and
prior authorization requirements, and formularies that
exclude branded drugs and limit formulary coverage to gen-
eric drugs in certain therapeutic categories. Automatic state
generic substitution laws, which allow pharmacists to substi-
tute generic drugs for brand-name drugs, so long as physi-
cians have not specified that the brand-name drug
prescription must be “dispensed as written” have also been
key factors in the increased use of generic drugs.

This study provides an additional update in a series of
periodic studies by the authors of evidence on recent trends
in three factors that have a potentially substantial influence
on the balance of cost savings and incentives for continued
inflation in the form of new drugs: (1) MEPs for new
brand-name drugs; (2) the probability, timing, and number
of patent challenges faced by brand-name drugs under
Paragraph IV of the Hatch–Waxman Act; and (3) the rate and
extent of generic drug penetration following initial generic
entry. As previously, our analysis is restricted to the U.S.,
the largest brand-name drug market. Laws, regulations, pre-
scribing practices, and the economic context for generic
drugs in other countries differ.

Methods

Data sources

IQVIA National Sales Perspectives data were used to calcu-
late MEPs for brand-name drugs experiencing first generic
entry in the U.S. between January 2015 and December 2019.
This is the same data source relied on for the prior analyses
in this series, and the data obtained for this study was
merged with similar data for the period 1995 through
September 2012, and October 2012 through December 2014. Consistent with prior practice, data for an overlap period (November 2013 through December 2014) were reviewed, and where there were updates to previous values for a given drug, they were incorporated. The data set used in the analysis contained information about all brand-name drugs experiencing first generic entry during this period (as defined by IQVIA-defined generic sales), including new molecular entities (NMEs) and new formulations of older drugs (which include changes in the form of administration, such as the availability of an oral solid pill rather than an injected form, but exclude new strengths, such as a 15 milligram rather than 30-milligram pills). New labeled indications not accompanied by changes in the form of administration or strength are excluded. As in prior published analyses in this series, our analysis is limited to NMEs. Likewise, and consistent with prior analyses, we restrict our analysis to those drugs subject to ANDA generic entry under the Hatch–Waxman Act, and we exclude drugs subject to biosimilar entry under the Biologics Price Competition and Innovation Act (BPCIA), which defines a regulatory pathway for biosimilars in the U.S. Others have presented recent data on the evolving U.S. biosimilar market.10

We restrict the MEP calculations to just NMEs experiencing first generic entry by a drug determined to be therapeutically equivalent to the brand-name drug, introduced by an independent manufacturer (i.e., we do not include authorized generics in the MEP calculations marketed by the brand name drug company, or another company with the brand company’s permission, but a later generic introduced by an independent manufacturer for the same molecule would be counted). We present data only on the resulting 356 NMEs experiencing initial generic entry between January 1995 and December 2019. This figure of 356 NMEs excludes several products from the analysis for the following reasons: a generic drug version was subsequently withdrawn as a result of litigation after initial generic entry (one product), and FDA approval of the original brand-name drug occurred prior to October 1962 and the safety and efficacy data requirements introduced at that time (eight products).

The data analyzed includes information on unit and dollar sales and dates, as well as information on characteristics such as mode of administration and the number of generic entrants. All sales data are presented in 2008 dollars, adjusted using the U.S. Department of Labor’s Consumer Price Index for All Urban Consumers (CPI-U), in order to allow direct comparison with previous analyses in this series.

To identify all of the drugs in the MEP data set for which there was a Paragraph IV ANDA filing and the date of the first filing for each drug, we reviewed information from the FDA’s website on Paragraph IV ANDA filings, ANDA approval letters in the study period, and other public information searches. We used data from ParagraphFour.com to determine the number of Paragraph IV challengers. ParagraphFour.com, a specialized proprietary data aggregator, collects information from patent litigation court filings related to Paragraph IV ANDA submissions. The data include a list of ANDA-filing generic manufacturers who are defendants in such filings. For each NME, we counted the number of unique ANDA-filing generic manufacturer defendants listed in patent litigation court filings and recorded that as the number of Paragraph IV challengers for that NME. As noted, while generic drug companies may file ANDA challenges for multiple product strengths (e.g., 15 milligrams and 30 milligrams) for a given NME, we counted each ANDA-filing generic manufacturer patent litigation defendant only once (therefore, the total number of challenges faced by the NME for all of its strengths may be higher). Because we rely on ParagraphFour.com data derived from patent litigation filings, our counts exclude instances where generic manufacturers filed a Paragraph IV ANDA, but there were no patent litigation court filings. As in prior analyses, our data only reflect drugs that have experienced generic entry; drugs where there was a Paragraph IV ANDA filing, but where generic entry has not yet occurred are excluded from this analysis and would be captured in future analyses.

For the subset of drugs in our sample that experienced first generic entry between 1999 and December 2019, we reviewed IQVIA National Sales Perspectives (NSP) monthly data on standard units for the brand-name drug and for generic versions of the drug (including authorized generics, which may be marketed by the brand name drug company, or another company with the brand company’s permission). According to IQVIA, NSP data reflect sales from manufacturers or wholesalers to pharmacies, clinics, hospitals and other healthcare providers, and represent 100% coverage of retail and non-retail channel sales.10 Because the monthly sales data series was available beginning in 1999, our calculations of the monthly erosion of brand-name drugs’ share of standard units for the twelve months after the first generic entry began then. For the NMEs experiencing first generic entry in 2019 and where twelve months of data following the first generic entry were not available as of December 2019, we calculated generic erosion rates for the available months. The extent of brand-name drug share erosion is summarized based on the timing of first generic entry (by two-year cohorts, or three-year cohort in the case of 2017–2019), illustrating the increasing extent of brand-name drug erosion for drugs over time.

Methods

Consistent with prior versions of this research, we defined the MEP as the time between the market launch of a brand-name drug (as measured by its first reported sales) and the market launch of its first A-rated generic competitor (i.e., a generic drug characterized by the FDA as therapeutically equivalent, having demonstrated bioequivalence to the branded drug) to any strength of the brand-name drug. For purposes of the analysis, A-rated authorized generics were excluded from the determination of when the MEP ended but were included in the generic erosion calculations. As a result, the MEP of a given drug reflects the interaction among many technical, regulatory, and competitive factors, any one or more of which can lengthen or shorten it. These factors include: when patent filings occur; eligibility for
patent term restoration and how much patent term is lost during product development and clinical testing and during FDA regulatory review before approval; whether one or more generic patent challenges occur and the outcome of those challenges (including the timing of stays on generic entry for up to thirty months pending court decisions on patent infringement suits); and the market entry decisions of generic manufacturers, and how long the FDA review of their generic applications take.

Consistent with prior studies in this series, we calculate and present the average number of generic entrants within one year of first generic entry by the level of sales in the year prior to generic entry (i.e. less than $100 million, greater than or equal to $100 million and less than $250 million, greater than or equal to $250 million and less than $1 billion, and $1 billion or larger). For ease of direct comparison with the results of prior research, sales figures are inflation-adjusted to 2008 dollars using the U.S. Department of Labor Consumer Price Index for All Urban Consumers (CPI-U). As a reference, sales of $250 million in 2008 dollars correspond to just over $300 million in 2020 dollars. Results are presented in tables and figures according to the cohort of the initial generic entry period (i.e. drugs experiencing first generic entry in 1995–1998, 1999–2002, 2003–2006, 2007–2010, 2011–2014, and 2015–2019).

The share of NMEs experiencing Paragraph IV filings for a given year (i.e. Paragraph IV filing frequency) is defined as the number of NMEs experiencing at least one Paragraph IV filing for any strength of that brand-name drug at any time prior to the first generic entry, divided by all NMEs in the dataset experiencing first generic entry in the same year. Results are presented by year of first generic entry. As noted earlier, NMEs may experience Paragraph IV challenges for more than one strength of the same drug, and the time from NME launch to the first Paragraph IV filing for any strength was defined as the Paragraph IV timing. The number of Paragraph IV challengers was defined as the number of unique generic manufacturers filing ANDA challenges for at least one strength for the NME. As noted, these counts are limited to those in which generic entrants face patent litigation from the brand-name manufacturer, based on data from ParagraphFour.com for the years 2004 through 2019. Because ParagraphFour.com data are sourced from patent litigation complaints associated with Paragraph IV ANDA filings, calculations of the average number of challengers are restricted to the NMEs where patent litigation filing data are available. For the period 2015 through 2019, the ParagraphFour.com data is augmented with information from the FDA on the number of substantially complete Paragraph IV ANDA submissions. Overall, data on the number of Paragraph IV ANDA challengers were identified for 96% of NMEs in the data set with challenges and first generic entry between 2004 and 2019.

The generic penetration rate was defined as the number of units of the drug that are filled by a generic version of the drug rather than by the brand-name drug, divided by the total units of that molecule (including both brand-name and generic version). Generic penetration rates reflect market factors, an increase over time in the mechanisms available to commercial insurance and public plans to promote generic use, as well as state regulations and laws. As noted, all A-rated generics, including authorized generics, are included in the generic penetration rate calculations.

All figures are unweighted averages, with standard deviations presented in parentheses. Paragraph IV filing frequency and timing calculations presented in Figures 3(A) for all NMEs and 3B (for NMEs with sales>$250 million in the twelve months before generic entry) are three-year moving averages. Sales figures are expressed in 2008 dollars.

Results

Average period of market exclusivity

Figure 1 shows the average length of the market exclusivity period for all new drugs and for NMEs>$250 million, by year of first generic entry. Between 1995 and 2019, the average MEPs for all drugs experiencing first generic entry ranged between 12.2 and 14.6 years over the period, and between 10.1 and 13.7 for NMEs>$250 million.

NMEs>$250 million represent 42 percent of all drugs and 92 percent of sales for all drugs in our data set experiencing generic entry. The average MEP for NMEs>$250 million was 13.0 years in the most recent period in our study (2017–19) and 14.1 years for all NMEs (the corresponding figure for NMEs<$250 million was 15.6). The corresponding median figures were 14.3 years for NMEs>$250 million for the most recent period (2017–19) and 14.5 years for all NMEs. The corresponding median figure for the NMEs<$250 million for the most recent period was 15.3. Figures for each cohort of NMEs, as defined by the year of first generic entry, are presented in Table 1.

Figure 2 shows the average number of generic competitors in the twelve months after the first generic entry. Results are presented by sales level and by year of first generic entry. In each first generic entry-year cohort, the average number of generic entrants is highest for drugs with the highest sales before the first generic entry. For example, for branded drugs experiencing first generic entry in the years 1995–98, there was one drug with over $1 billion in annual sales prior to generic entry (in 2008 dollars), and there were six generic entrants after one year. For branded drugs experiencing first generic entry in the years 1999–2002, there was an average of between 11 and 12 generic entrants, 7 and 8 for 2003–06, 12 and 13 for 2007–10, 9 and 10 for 2011–14, and 9 and 10 for 2015–19.

Paragraph IV challenges

The probability of facing a Paragraph IV challenge has increased steadily over time, both for all NMEs (Figure 3(A)) and higher-sales drugs (NMEs>$250 million in 2008 dollars, Figure 3(B)). For all NMEs, just 9 percent of drugs experiencing first generic entry in 1995 had faced any Paragraph IV challenge by the time of the launch of the first generic. For drugs experiencing first generic entry in 2019, the figure had
increased to 81%. For higher-sales drugs (NMEs > $250 million in 2008 dollars), the probability of facing a Paragraph IV challenge reached 93 percent for drugs experiencing first generic entry in 2008. The corresponding figures for oral formulation drugs showed similar results, with the percentage facing Paragraph IV challenges increasing from 6 percent in 1995 to 81 percent in 2019 (data not shown). All percentages in Figures 3(A,B) are three-year moving averages.

Figures 3A and 3B also show that branded drugs face Paragraph IV challenges earlier after launch. The average time between launch and facing the first Paragraph IV challenge was 18.7 years for all drugs and 14.3 years for NMEs > $250 million (one drug) for branded drugs experiencing first generic entry in 1995 (that faced at least one Paragraph IV challenge by the time of first generic entry). For drugs experiencing first generic entry in 2019, the corresponding figures were 6.3 years for all drugs and 6.0 years for NMEs > $250 million (three-year moving averages).

The average number of Paragraph IV challengers per NME varies by year of first generic entry, ranging between 2.8 (2005) and 8.6 (2018). The number of unique challengers for an NME ranged between one and 25, averaging 5.5 for the years 2004–19. Data on the probability of Paragraph IV challenges, time to the first Paragraph IV challenge, and the number of challengers, by year of first generic entry, are presented in Table 2.

The values presented in Figures 3(A,B) are three-year moving averages for all NMEs, by year of first generic entry. The probability of a Paragraph IV filing, the time to first-Paragraph IV filing, and the number of Paragraph IV challengers for an individual NME may be affected by the level of sales, the manufacturing challenges involved (e.g. for different formulations), and other factors. Paragraph IV challenges may be more likely for higher-revenue drugs; even a low probability of litigation success may be associated with an attractive return on the investment involved in the patent challenge. For instance, others have found previously that Paragraph IV challenge court decisions involved a disproportionate share of drugs with high sales (results for those filed prior to 2005)12. In addition, other researchers have reported that with increases in brand-name drug sales, the probability of success required to justify a patent challenge reaches less than 1%13. Brand companies prevailed in just over half (54%) of district court patent cases decided between 2009 and 201214.

Table 3 presents our similar findings that controlling for year of brand launch and form (i.e. oral, injectable, other non-oral), higher brand sales twelve months prior to first generic entry are associated with a significantly higher probability of facing a Paragraph IV filing, a shorter time to the first Paragraph IV filing, and a higher number of challengers. For instance, five-fold increases in branded drug sales (in
in the twelve months prior to first generic entry (e.g. from $100 million to $500 million), holding all other variables constant, was associated with an approximate 14 percentage point increase in the probability of the branded drug facing a Paragraph IV challenge. It was also associated with roughly a seven-month shorter period to the first Paragraph IV filing and 1.2 additional ANDA challengers (figures are marginal effects for the average drug, evaluated at the means of other variables).

Market share erosion after generic entry

Generic erosion, or the share of all units sold represented by generics rather than the branded drug, has increased dramatically since 1999–2000. Figure 5 displays the brand-name drug share for the twelve months following the first generic entry. Brand share is defined as the number of standard units of the branded drug divided by the sum of the number of standard units of branded drugs and their generics. For all NMEs facing first generic entry in 2017–19, brand share averaged only 23 percent of standard units twelve months after the first generic entry. For NMEs>$250 million, branded drug share was only 18 percent of standard units at one year (data not shown).

In comparison, brand-name drugs experiencing their first generic entry in 1999–2000 maintained a share of 44 percent of units at one year following the first generic entry. Grouping drugs into two-year cohorts by the date of first generic entry (three years in the case of 2017–19) shows the increase in the rate and extent of generic penetration over the past two decades.

Discussion

Our findings extend and expand upon closely-related research originally conducted by Grabowski and Kyle (2008)\(^5\), and updated for subsequent periods in Grabowski, Kyle, Mortimer, Long, and Kirson (2011)\(^6\), Grabowski, Long and Mortimer (2014)\(^7\), and most recently, Grabowski, Long, Mortimer and Boyo (2016)\(^8\). The most recent previous analysis in this series calculated MEPs for NMEs experiencing first generic entry between 1995 and December 2014. Extending this continuous data series, we include here data on NMEs experiencing first generic entry through December 2019, consistently derived using the same data sources and methods. As in the prior analyses, we present results for all NMEs, as well as for those with sales greater than $250 million (in 2008 dollars) in the year before generic entry.

MEPs for higher-sales drugs have remained relatively constant for nearly the past decade, averaging 13.0 years for NMEs>$250 million experiencing initial generic entry in 2017–19, and 14.1 years for all NMEs (for NMEs<$250 million, the corresponding figure was 15.6 years). While the average MEP for brand-name drugs has remained relatively constant, particularly for molecules with higher sales, generic manufacturers generally continue to file Paragraph IV challenges more often and earlier than in the earlier years of this time series, which begins with drugs experiencing first generic entry in 1995. Because we calculate MEPs only for those branded drugs already experiencing generic entry, more frequent and earlier Paragraph IV challenges may exert a downward impact on MEPs in the future, other factors equal. For brand-name drugs experiencing first generic entry in 2019, 81 percent had faced at least one Paragraph IV patent...
challenge; for branded drugs experiencing first generic entry in 1995, the figure was only 9 percent. For higher-sales drugs (NMEs $250 million in 2008 dollars), 93 percent had faced at least one Paragraph IV challenge in 2019, up from 25 percent for higher-sales branded drugs experiencing first generic entry in 1995. (All figures are 3-year rolling averages)

Paragraph IV challenges continue to be filed relatively early on in the commercial life cycle of a branded drug — 6.3 years on average after brand launch for all NMEs, and 6.0 years on average after brand launch for NMEs $250 million. NMEs facing a Paragraph IV patent challenge over the most recent period (2017–19) faced an average of 6.8 challengers. Most NMEs faced more than one patent challenge; 79 percent of NMEs challenged faced more than one challenger. As noted, NMEs may experience more total challenges (and unique challengers) when challenges to multiple strengths for the same drug are taken into account.

Other analysis by one of the co-authors of litigation data confirms that there is a statistically significant downward effect of patent challenges on MEPs, all other factors equal, and finds that top-selling drugs (top-quintile sales) have experienced a statistically significant downward trend in projected MEPs over time15.

Generic competition has intensified over the past two decades. For NMEs $250 million experiencing initial generic entry in 2017–19, the average unit share of the branded drug had fallen to just 18 percent twelve months after first generic entry; for all NMEs the figure was 23 percent.
Table 2. Paragraph IV filing frequency, timing, and number of challengers.

| Year of first generic entry | All NMEs                           | NMEs with sale greater than $250 million |
|-----------------------------|------------------------------------|------------------------------------------|
|                             | 3-year moving average              | 3-year moving average (SD)               |
|                             | Share with PIV filing | Time to PIV filing | No. of challengers, mean | Share with PIV filing | Time to PIV filing | No. of challengers |
|-----------------------------|------------------------------|-------------------|-------------------------|--------------------------|-------------------|-------------------|
| 1995                        | 9% (0.29)                     | 18.7 years (NA) | 25% (0.25)              | 14.3 years (NA)          |
| 1996                        | 14% (0.34)                    | 15.6 (5.4)       | 25% (0.31)              | 12.5 (NA)                |
| 1997                        | 19% (0.38)                    | 15.8 (8.6)       | 8% (0.14)               | 10.7 (NA)                |
| 1998                        | 31% (0.45)                    | 10.3 (6.2)       | 42% (0.14)              | 8.3 (0.3)                |
| 1999                        | 32% (0.46)                    | 12.2 (7.3)       | 47% (0.16)              | 7.9 (1.3)                |
| 2000                        | 38% (0.48)                    | 9.7 (4)          | 74% (0.29)              | 7.6 (1.6)                |
| 2001                        | 38% (0.48)                    | 10.8 (4.8)       | 56% (0.45)              | 8.1 (2.8)                |
| 2002                        | 47% (0.5)                     | 8.4 (3.3)        | 76% (0.29)              | 6.7 (2.9)                |
| 2003                        | 44% (0.49)                    | 8.4 (4.1)        | 70% (0.32)              | 7.3 (3.4)                |
| 2004                        | 41% (0.48)                    | 7.7 (3.9)        | 65% (0.31)              | 7.0 (2.7)                | 3.0 (1.5)         |
| 2005                        | 42% (0.48)                    | 8.4 (3.5)        | 60% (0.42)              | 8.5 (2.8)                | 5.5 (4)           |
| 2006                        | 47% (0.49)                    | 8.5 (3.1)        | 62% (0.42)              | 8.0 (2.8)                | 5.7 (4.1)         |
| 2007                        | 60% (0.47)                    | 8.5 (3.1)        | 86% (0.27)              | 7.8 (2.9)                | 7.2 (6)           |
| 2008                        | 65% (0.46)                    | 8.0 (3.6)        | 81% (0.3)               | 7.5 (3.4)                | 6.7 (5.6)         |
| 2009                        | 68% (0.46)                    | 8.3 (3.4)        | 87% (0.26)              | 8.0 (2.7)                | 5.7 (5.5)         |
| 2010                        | 68% (0.46)                    | 8.2 (3.5)        | 81% (0.38)              | 8.5 (3.2)                | 6.6 (5.3)         |
| 2011                        | 73% (0.43)                    | 7.9 (5)          | 91% (0.23)              | 7.5 (2.7)                | 4.2 (4.1)         |
| 2012                        | 75% (0.42)                    | 7.1 (2.7)        | 89% (0.25)              | 6.6 (NA)                 | 8.0 (5.5)         |
| 2013                        | 77% (0.41)                    | 7.2 (2.5)        | 94% (0.12)              | 6.5 (2.5)                | 7.1 (4.3)         |
| 2014                        | 73% (0.43)                    | 7.0 (2.5)        | 85% (0.27)              | 6.3 (2.3)                | 5.2 (2.5)         |
| 2015                        | 78% (0.41)                    | 7.0 (3)          | 90% (0.15)              | 6.3 (2.7)                | 11.4 (7.9)        |
| 2016                        | 81% (0.38)                    | 6.6 (3)          | 87% (0.26)              | 5.8 (2.4)                | 6.7 (3.3)         |
| 2017                        | 82% (0.37)                    | 6.5 (3.4)        | 92% (0.22)              | 6.0 (2.5)                | 8.8 (6.5)         |
| 2018                        | 84% (0.35)                    | 6.3 (3)          | 92% (0.22)              | 5.8 (2.4)                | 11.7 (8.7)        |
| 2019                        | 81% (0.39)                    | 6.3 (3.3)        | 93% (0.17)              | 6.0 (2.7)                | 7.1 (5.9)         |

Source: IQVIA data on all new drugs with an initial generic entry in the period 1995 through December 2019. Food and Drug Administration data, ParagraphFour.com data and general public information sources on Paragraph IV challenges.

Notes: New molecules with sales greater than $250 million based on sales in the year prior to generic entry and inflation-adjusted to 2008 dollars using the Consumer Price Index for All Urban Consumers. Figures in parentheses are standard deviations.

Time to Paragraph IV filing is measured as the number of years from brand launch to the first Paragraph IV filing. In years where only one or no NMEs experienced a Paragraph IV filing, it is not possible to calculate the standard deviation for the time to PIV filing. In these cases, the standard deviation is recorded as NA.

Figure 4. Paragraph IV challengers by year of first generic entry 2004–2019.
Conclusions

The MEP is a key financial metric for brand-name drugs – branded drug manufacturers rely on profits earned during the market exclusivity period (MEP), and brand-name drug shares drop steeply after the first generic entry. The average MEP for brand-name drugs, 13.0 years for NMEs with pre-generic entry sales of at least $250 million (in 2008 dollars) and 14.1 years for all drugs, for the most recent period, remains roughly consistent with prior research, particularly for higher-sales drugs. MEPs are lower and Paragraph IV challenges are more frequent and occur earlier for NMEs >$250 million. Over the past two-and-a-half decades, branded drug manufacturers face Paragraph IV challenges increasingly frequently, and they face them earlier in the branded drug’s commercial life cycle. Most NMEs experience multiple Paragraph IV patent challenges. Generic erosion of branded drug share remains rapid and deep, for all NMEs and NMEs >$250 million.

Note

i. IQVIA Holdings, Inc.; Danbury, CT, USA.

Transparency

Declaration of funding

Analysis Group, Inc. received financial support from the Pharmaceutical Research and Manufacturers of America for this research. HG received no financial support.
Declaration of financial/other interests

Three of the authors (GL, RM, MB) were employees of Analysis Group, Inc. at the time of the research, a consulting company that has provided services to biopharmaceutical manufacturers, both brand-name and generic. HG has served as an expert witness in pharmaceutical patent-related litigation on behalf of both plaintiffs and defendants. The analysis presented was designed and executed entirely by the authors, and therefore, they are responsible for any errors or misstatements.

JME peer reviewers on this manuscript have received an honorarium from JME for their review work, but have no other relevant financial relationships to disclose.

Author contributions

HG, GL and RM contributed to the conception and design of the study. All authors contributed to the analysis and interpretation of the data, the drafting and revising of the manuscript, and gave final approval of the manuscript to be published. All authors agree to be accountable for the aspects of the work as described above.

Acknowledgements

No assistance in the preparation of this article is declared.

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