Journal of Medical Economics ›
Volume 17, 2014 - Issue 3

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Professional: Brief report

Recent trends in brand-name and generic drug competition

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Pages 207-214 | Accepted 06 Dec 2013, Published online: 23 Dec 2013

Cite this article https://doi.org/10.3111/13696998.2013.873723

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IMS Hea r the 257
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approval letters, the FDA website, and public information searches to identify drugs experiencing Paragraph IV filings, and the first filing date.

Results:

For drugs experiencing initial generic entry in 2011–2012, the MEP was 12.6 years for drugs with sales greater than $100 million (in 2008 dollars) in the year prior to generic entry, 12.9 years overall. After generic entry, the brand rapidly lost sales, with average brand unit share of 16% at 1 year; 11% for NMEs with pre-generic entry sales of at least $250 million (in 2008 dollars). Over 80% of NMEs experiencing 2011–2012 initial generic entry had faced at least one Paragraph IV challenge from a generic manufacturer. These challenges were filed relatively early in the brand-name drug life cycle: within 7 years after brand launch, on average.

Limitations:

Analyses, including Paragraph IV calculations, were restricted to NMEs where generic entry had occurred.

Conclusion:

Pharmaceutical competition continues to evolve; while the average MEP below 13 years for 2011 ges are increasi sified.

Keywords

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Intro

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system where new brand-name drugs generate nearly all of their sales during a market exclusivity period (MEP, the time period between market launch of a brand-name drug and the launch of its first generic), generic manufacturers frequently challenge patents protecting brand-name drugs, and generic drugs tend to rapidly supplant sales of the corresponding brand-name drug following generic entry.

The Hatch-Waxman Act included a number of provisions aimed at facilitating approval of generic drugs by the Food and Drug Administration (FDA) and encouraging generic entry (and other provisions encouraging innovation described later below). One of the primary provisions of the Act established an Abbreviated New Drug Application (ANDA) process, which greatly reduced the cost of completing an FDA application for approval of a generic drug. Prior to the Hatch-Waxman Act, generic manufacturers were required to submit original safety and efficacy data on their products to gain market approval by the FDA. To meet this requirement, the generic manufacturer generally had to duplicate many of the brand-name manufacturer's trials[1]. Under the ANDA process, generic manufacturers need only demonstrate that their products have the same active ingredients as and are 'bioequivalent' to their brand-name counterparts. Generic manufacturers also received a research exemption for bioequivalence studies, allowing them to begin research on the innovator's drug prior to patent expiration, without running afoul of patent law.

The Hatc o challenge brand-na ragraph IV challeng e FDA that it claims it -name drug, or that a e drug manufac ny within 45 days of r ot approve the g settlement, or unti entive for generic manufacturer (or manu approval of its appli -day period of exclus d generic version a dosage form or ed by the

on the same day. A generic manufacturer's 180-day exclusivity period applies only to the dosage form or strength level for which that manufacturer was the first to file a Paragraph IV challenge.

The 180-day period of exclusivity generally is very profitable to a generic manufacturer because the generic manufacturer tends to drop price only modestly below the brand price during this period, generic share increases rapidly, and generic sales are enjoyed by a single manufacturer (or a few first-filing manufacturers). This provides substantial incentives for being the first to file a Paragraph IV challenge, or being among the first-filers.

In an effort to balance these provisions aimed at encouraging more generic competition for brand-name drugs, the Hatch-Waxman Act also established new incentives for innovation for brand-name drug manufacturers. For example, innovators can receive an additional period of patent protection through so-called patent term restoration. This provision extends the life of a patent on a drug by up to 5 years, with the aim of compensating for time that the innovator company spent conducting human clinical trials on the drug before it applied to the FDA for approval of the drug through a New Drug Application (NDA) and also for a portion of the time the NDA is under FDA review. Under patent term restoration, the life of the patent cannot be extended by more than 5 years, and the remaining patent term after FDA approval cannot exceed 14 years, including

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coverage to generics in certain therapeutic categories[2,3]. In addition, a number of state laws allow generic forms to be substituted automatically by pharmacists for brand-name drugs prescribed by physicians, so long as physicians have not specified that the prescription must be 'dispensed as written'. As a result, generic products' share of total prescriptions in the US increased from 36% in 1994 to 84% in 2012[4].

The impact of Hatch-Waxman on incentives to innovate has received somewhat less attention. A 1998 report by the Congressional Budget Office estimated that generic competition reduces by 12% the net present value of the total stream of future profits expected from the average brand-name drug. In particular, the Congressional Budget Office found that, for brand-name drugs, the negative effects on returns from generic competition probably outweighed the positive effects of patent term restoration, described above[5].

The objective of this study was to provide evidence on recent trends in three factors that have a potentially substantial influence on the balance of cost savings and incentives for continued innovation in the form of new drugs: (1) MEPs for new brand-name drugs; (2) the likelihood and timing of Paragraph IV patent challenges under the Hatch-Waxman Act, through which generic manufacturers challenge the validity or applicability of patents protecting brand-name drugs; and (3) the rate and extent of generic drug penetration following initial generic entry.

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IMS Health National Sales Perspectives data were used for calculating MEPs for drugs experiencing first generic entry between January 2007 and September 2012. This is the same data source relied on for prior analyses, and the data obtained for this study was merged with similar data for the time period 1995–2006. The data set used in the analysis contained information about all 460 drugs experiencing first generic entry during this period, including 257 NMEs, and 203 new formulations of older drugs. New formulations include changes in the form of administration—for example, changing from an injection to a topical application—but not new strengths or new indications. We excluded several products from the analysis based on the following criteria: one product was excluded because generic versions of it were subsequently withdrawn as a result of litigation following initial entry; and seven products were excluded because the original brand FDA approval pre-dated October 1962 and the requirements for safety and efficacy data introduced at that time. Our analysis focused on NMEs and we present data only on the 257 NMEs experiencing initial generic entry between January 1995 and September 2012 because regulations for generic entry differ if the brand-name product is a new formulation.

In addition to providing the information necessary to calculate MEPs, the data also included information on drug characteristics, such as mode of administration and number of generic entrants. All sales data are presented in 2008 dollars, adjusted using the US D rs as the market c

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brand-name drugs' share of standard units for the 12 months following first generic entry. The extent of brand-name drug share erosion is summarized based on the timing of first generic entry, illustrating the increasing extent of brand-name drug erosion for drugs more recently experiencing first generic entry.

Methods

Consistent with prior research, we defined the MEP as the time between the launch of a brand-name drug and the launch of its first generic competitor. As noted, this definition reflects the often complex interaction among many technical, regulatory, and competitive factors, including: the timing of patent filings, the amount of patent term lost during product development, the duration of regulatory review before FDA approval, the eligibility for patent term restoration under the Hatch-Waxman Act, the likelihood and outcome of generic patent challenges (including the possibility of a stay on generic entry for up to 30 months pending court decisions on patent infringement suits), entry decisions by generic manufacturers, and the duration of FDA review of generics. Any one or a combination of these factors can affect the market exclusivity of a particular drug. The average MEP remains a key determinant of profitability and incentives for innovation.

The average number of generic entrants within 1 year of first generic entry was calculate al to $100 million a d less than $1 billio ntry and inflation- mer Price Index fo e., 1995–1998, 19

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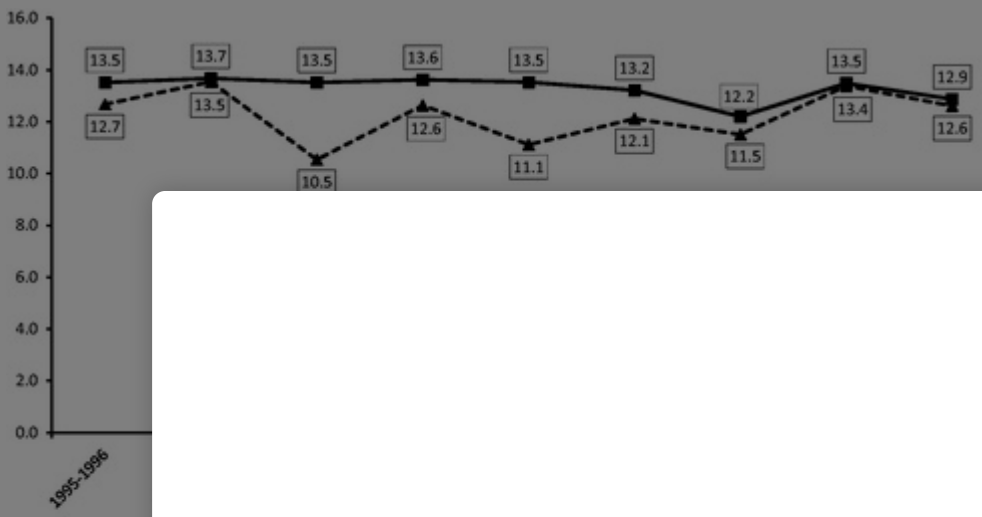
All figures presented are unweighted averages. Figures in parentheses following calculated averages are standard deviations. Figures for Paragraph IV filing frequency and timing (as presented in Exhibit 3) are 3-year moving averages.

Results

Average period of market exclusivity

Figure 1 shows the average length of the market exclusivity period for all new drugs, by year of first generic entry, and for those with annual sales greater than $100 million in the 12 months prior to generic entry (in 2008 dollars). Between 1995–2012, the average MEPs for all drugs experiencing first generic entry ranged between 12.2–13.7 years over the period.

Figure 1. Average market exclusivity period by year of first generic entry: new molecular entities.



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initial period (1995–1996). Figures for each cohort of NMEs, as defined by year of first generic entry, are presented in Table 1.

Table 1. Average market exclusivity period by year of first generic entry.

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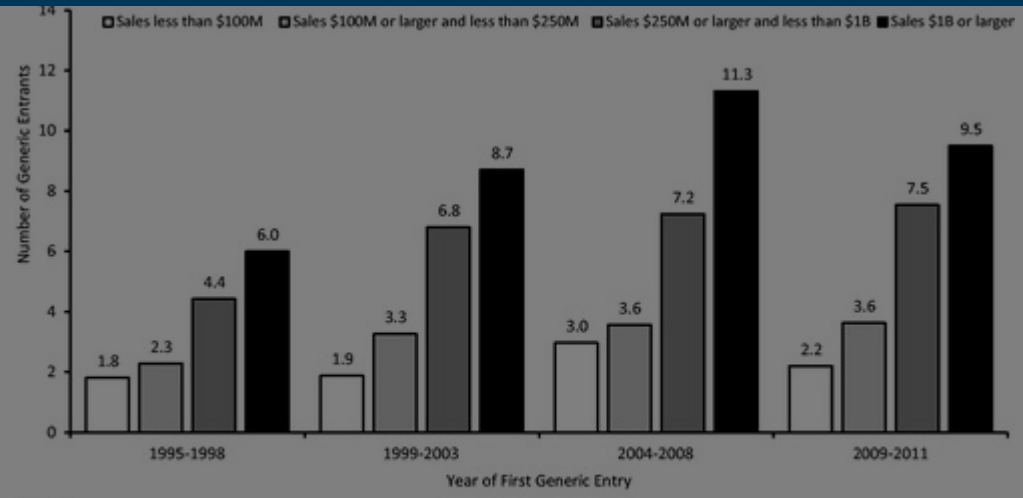
Average MEPs were similar whether we analyzed drugs with annual sales greater than $100 million, $250 million, or $1 billion (in 2008 dollars, data not shown).

Figure 2 summarizes the number of generic entrants observed for NMEs in the data. The exhibit shows the average number of a brand-name drug's generic competitors in the market 12 months after the first generic entry, segmented by level of sales and by time period. The number of generic entrants is higher for drugs with larger sales before the first generic entry and for drugs experiencing first generic entry after 1998. For example, one drug with over $1 billion in annual sales prior to generic entry experienced first generic competition in the period 1995–1998 and it faced six generic entrants after 1 year. The corresponding figures for drugs with over $1 billion in annual sales (in ght and nine ger 04–2008, and betwee c entrants were ex

Figure 2 entry: new molecul



Source:
IMS Health data on all new drugs with initial generic entry in the period 1995 through September 2012.
Notes:
New molecules with sales in the year prior to generic entry, inflation-adjusted to 2008 dollars using the Consumer Price Index for All Urban Consumers.

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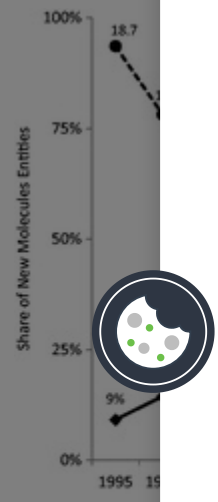
Paragraph IV challenges

The likelihood of a Paragraph IV challenge being filed has increased substantially in recent years (Figure 3). Only 9% of drugs experiencing first generic entry in 1995 had experienced a Paragraph IV challenge at any point prior to first generic launch. That share increased steadily to 81% by drugs experiencing first generic entry in 2012. Drugs with sales greater than $100 million the year before first generic entry (in 2008 dollars) faced an even higher probability of a Paragraph IV filing, increasing from 17% in 1995 to

Figure 3.



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Paragraph IV challenges also occur sooner following the launch of a brand-name drug (Figure 3). For drugs experiencing first generic entry in 1995 and also experiencing a Paragraph IV challenge, the average time between launch and the first Paragraph IV challenge was 18.7 years (6.2). That time fell to 6.9 years (3.4) for drugs experiencing first generic entry in 2012. For new drugs with sales greater than $100 million in the 12 months before first generic entry (in 2008 dollars), the time between brand launch and first Paragraph IV challenge fell from 14.3 years (one drug) in 1995 to 5.9 years (2.7) for 16 drugs in 2012 (data not shown). Paragraph IV challenge activity is even more aggressive for new drugs with sales greater than $250 million (in 2008 dollars). Of these drugs that experienced first generic entry in 2012, 92% also experienced a Paragraph IV challenge (13 of 14 drugs), and the average time from launch to first challenge was 6.3 years (3.0).

The calculations reflected in Figure 3 reflect averages across all new drug introductions associated with first generic entry in a given year. They may vary according to factors such as the drug's sales prior to generic entry, the nature of the patents protecting the drug, and the ease with which generic manufacturers can imitate the drug to satisfy FDA regulations. In particular, for higher-revenue drugs, generic manufacturers may be less selective when filing challenges, as even a low likelihood of success in litigation can yield a large expected return on the investment necessary to challenge a patent. For insta hallenges filed pric 9. Others have cal y of success required to below 1%10. F 009, brand compani between 2009–20

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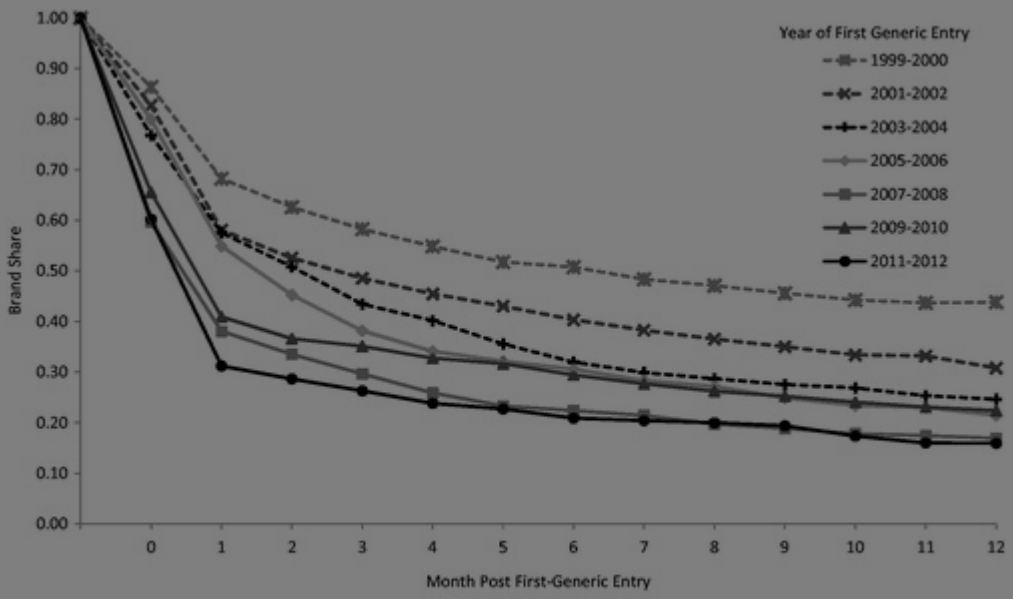
Figure 4 llowing first generic lecule divided and-name share of ained relativel st decade. For all N erage of only

2008 dollars) prior to first generic entry, generic erosion was even more pronounced; the corresponding figure was only 11% (0.09) of units at 1 year.

Figure 4. Average monthly brand share of standard units of the molecule/form following first generic entry.



Source:
IMS Health data for all new molecular entities with first generic entry in the period 1999 through September 2012.
Note:
Initial generic entry occurs at some point during month "0". Month "1" is the first full month of generic competition.

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In comparison, drugs experiencing first generic entry in 1999–2000 maintained a share of 44% (into 2-year periods ne rate and extent o

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following initial generic entry. For NMEs experiencing initial generic entry in 2011–2012 and with pre-generic entry sales of at least $250 million (in 2008 dollars), average brand unit share had fallen to 11% at 1 year; for all NMEs with initial generic entry in 2011–2012, average brand unit share at 1 year had fallen to 16%.

While the average MEP for brand-name drugs has remained relatively constant over the past 10–15 years, generic manufacturers are challenging the patents protecting brand-name drugs more often and earlier, which may have a downward impact on future MEPs (we calculate MEPs only for those already experiencing generic entry). Over 80% of brand-name drugs experiencing initial generic entry in 2012 had faced at least one Paragraph IV patent challenge from a generic manufacturer, up from only 9% for drugs experiencing initial generic entry in 1995. These challenges are filed relatively early in the brand drug life cycle, on average within 7 years of brand launch.

Conclusions

Pharmaceutical competition continues to evolve since the passage of the Hatch-Waxman Act in 1984. While the average MEP for brand-name drugs, currently 12.6 years for NMEs with pre-generic entry sales of $100 million (in 2008 dollars) and 12.9 years fo esearch, other fac have become has intensifi

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Two of the authors (Long and Mortimer) are employees of Analysis Group, Inc., a consulting company that has provided consulting services to biopharmaceutical manufacturers, both brand-name and generic. Henry Grabowski has served as an expert witness in pharmaceutical patent-related litigation on behalf of both plaintiffs and defendants. JME Peer Reviewers on this manuscript have no relevant financial or other relationships to disclose.

Acknowledgments

The authors thank Anna Kaltenboeck of Analysis Group, Inc. for research and technical assistance in the preparation of this article.

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