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Evergreening, patent challenges, and effective market life in pharmaceuticals☆

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ABSTRACT

Observers worry that generic patent challenges are on the rise and reduce the effective market life of drugs. A related concern is that challenges disproportionately target high-sales drugs, reducing market life for these "blockbusters."

To study these questions, we examine new data on generic entry over the past decade. We show that challenges are more common for higher sales drugs. We also demonstrate a slight increase in challenges over this period, and a sharper increase for early challenges. Despite this, effective market life is stable across drug sales categories, and has hardly changed over the decade.

To better understand these results, we examine which patents are challenged on each drug, and show that lower quality and later expiring patents disproportionately draw challenges. Overall, this evidence suggests that challenges serve to maintain, not reduce, the historical baseline of effective market life, thereby limiting the effectiveness of "evergreening" by branded firms.

1. Introduction

A central challenge in health policy is the calibration of pharmaceutical patent laws to optimize the balance between innovation and access. In the United States, Congress set this balance by enacting the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as the Hatch–Waxman Act. The Act is credited with a sharp subsequent increase in generic drug use, from less than 20 percent of prescriptions in 1984 (Frank, 2007) to 78 percent in 2010 (IMS Institute for Healthcare Informatics, 2011).

Part of the increase is due to a regulatory pathway permitting generic drug makers to challenge branded drug makers' patents, with a view to securing early Food and Drug Administration (FDA) approval and market entry. These patent challenges, which take the form of generic drug applications with so-called "Paragraph IV" certifications, provide a means for a generic firm to pursue entry when, in its view, the relevant patents are invalid or do not cover the proposed generic product.

Patent challenges are perhaps the most controversial feature of the Hatch–Waxman regime. The received wisdom is that challenges are on the rise, selectively target large sales drugs, and substantially reduce the effective market life of branded drugs. For example, Higgins and Graham (2009), writing in *Science*, worry that the rise in challenges shortens effective market life, and, by reducing the incentive to innovate, may contribute to the frequently noted dearth of new branded drugs. The generic strategy of frequent patent challenges has been given an evocative label, "prospecting" (Higgins and Graham, 2009; Grabowski and Kyle, 2007), which suggests a wide-ranging set of challenges filed in the hope of occasionally striking gold. The received wisdom has underpinned proposals from the National Academy of Sciences, academics, and industry to increase the data exclusivity period, during which new drugs' patents cannot be challenged, to between 10 and 12 years (Goldman et al., 2011; Higgins and Graham, 2009; National Academy of Sciences et al., 2007).

At the same time, other observers have identified the increasing acquisition of additional patents by brand-name drug makers, often of doubtful validity or applicability, in order to delay generic competition (Engelberg et al., 2009). This activity has been given

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the equally evocative label of "evergreening" (Thomas, 2005; Kesselheim and Avorn, 2006). Later issued, later expiring patents tend to be weaker, in the sense that a court is less likely to conclude that they are valid and infringed by a competing generic product. They tend not to be patents that cover the active ingredient—what we call "AI patents"—but patents pertaining to ancillary aspects of the drug. In the case of the blockbuster antidepressant Paxil (paroxetine), for example, the branded drug maker secured 10 such patents. The last expiring patent would, unless challenged, have blocked generic competition until 2019, compared to a successful challenge that secured generic approval and entry in 2003. Such patenting strategies are part of a larger set of tactics, which also include new formulations and other product line extensions, that can lengthen market exclusivity for therapies facing generic entry (Huskamp et al., 2008).

These debates about prospecting and evergreening have been the subject of much policy attention, but little analysis. We examine the causes and effects of patent challenges using a unique dataset of all instances of first time generic approval between 2001 and 2010, linked with information about each drug's patents, patent challenges, and other characteristics. We restrict attention to drugs that contain a novel active ingredient, so-called new molecular entities, or NMEs. This choice is significant. Concerns about prospecting are heightened when it comes to NMEs, sometimes considered the most innovative drugs (National Institute for Health Care Management, 2002). At the same time, evergreening is a less important concern for these drugs than for product line extensions, i.e., reformulations of drugs where the active ingredient was previously approved. For a line extension, an AI patent is likely to expire at an earlier point after product approval, if the drug even has an AI patent in the first place. Thus, this study places a lower bound on the extent of evergreening and the role played by patent challenges in curbing its effects.

Our descriptive results show that challenges are much more common for higher sales drugs. We also demonstrate a slight increase in challenges over this period, and a sharper increase for early challenges (those commencing within five years of drug approval). Despite this, effective market life is stable across drug sales categories, and has hardly changed over the decade, despite predictions to the contrary in previous research.

A second set of analyses, exploiting variation within each drug, explains this surprising result. While drug sales matter for the likelihood that a generic firm launches a patent challenge, so do patent characteristics. Fixed effects models show that within drugs, lower quality patents and those that, unless challenged, extend market life the most, are much more likely to be challenged. Patent challenges are disproportionately targeting patents, especially low quality ones, that aim to extend patent term. There is some evidence, though limited, that generics are more aggressive in challenging the "basic" (AI) patents for more lucrative drugs. However, challenges to these patents do not generally result in earlier entry, suggesting that generic drug makers seldom win these challenges. Overall, and contrary to their portrayal in current policy debates, patent challenges appear to be playing a restorative role, by ratcheting back the effective market life of drugs with long nominal patent terms.

Section 2 describes how patent challenges work and reviews previous research that provides context for our analyses. Section 3 describes our data. Section 4 reports basic descriptive statistics and traces trends in patent challenges, nominal patent term, and effective market life over the past decade. Section 5 presents drug-level and patent-level regression results about the causes and effects of patent challenges. Section 6 concludes.

2. Regulatory background and previous research

After a branded drug maker places a patented drug on the market, a generic firm may seek to market a competing version of the same drug by filing an Abbreviated New Drug Application, or ANDA, with the FDA. If the generic firm chooses not to challenge any branded drug patents, the FDA delays approval until all patents expire. A generic firm seeking pre-expiration entry files an ANDA asserting that one or more patents are invalid or not infringed by the proposed generic product. To encourage these challenges, the Act provides a bounty to the first challenger, a period of 180 days of exclusivity during which other generics cannot enter.

At the same time, the Act delays the onset of this challenge process, by prohibiting a generic firm from filing an ANDA during the first four years after branded drug approval.[1] This "data exclusivity" period is extended in practice by the subsequent challenge and FDA approval process, which typically require several years to complete, even where the generic firm's patent challenge is eventually successful.

Grabowski and Kyle (2007) offer the first systematic empirical analysis of how challenges affect market life. They examine market life (what they call the "market exclusivity period") for NMEs with first generic entry between 1995 and 2005. In their sample, average market life is 13.5 years. They find that market life is decreasing in sales: NMEs with annual sales less than $50 million have average market life of 15.1 years, compared to 12.7 years for drugs with sales greater than $500 million. Market life is falling slightly over time (13.6 years for 1995–2000; 13.4 years for 2001–2005). The authors also report that the ten drugs in their sample with sales exceeding $1 billion have progressively shorter market life over time: 13.8 years in 1995–2001, compared to just 11.2 years in 2002–2005.

Grabowski and Kyle suggest that patent challenges—and challenges that occur earlier in the life of a branded drug—may have caused the overall shorter market life for high-sales drugs and the decrease over time for blockbusters.[2] The authors call this potential generic strategy "prospecting"—a metaphor that has proven influential in later work (Berndt et al., 2007a; Branstetter et al., 2011; Higgins and Graham, 2009)—and draw particular attention to challenges of major drugs that occur early in the market life of a new drug (p. 498). In their regression analyses, the authors find that drugs with patent challenges have between 1.2 and 1.6 years less market life, depending on the specification (significant at the 10 percent level).[3]

Other work has examined the effects of patent challenges on branded drug makers. Filson and Oweis (2010) use an event-study framework to assess the effects of two court decisions that made patent challenges more likely, finding that these decisions are associated with a lower propensity for startup firms to form alliances.

[1] The four-year delay is limited, with minor exceptions, to patented drugs that are new molecular entities. If the generic firm decides to wait until patent expiration, or there are no patents, the delay is five years.

[2] For example, with respect to blockbusters, the authors note, "[A]ll but a few of these billion dollar drugs over the 1995–2005 period have been subject to [patent challenges]. . . . The fact that these challenges are now occurring earlier in the product life cycle may be one of the significant factors explaining the tendency toward shorter [market exclusivity periods] in recent years" (p. 497). As for the longer life of low sales drugs, the authors note that these differences are not necessarily due to patent challenges, but could also reflect the unprofitability of generic entry on such drugs.

[3] Grabowski and Moe (2008) emphasize the growth of early challenges as a rationale for longer data exclusivity terms, noting that the current period "affords branded products a floor of effective exclusivity of 5 to 7 years," a period that offers "insufficient time for most new drugs to recoup the up-front R&D costs and earn a positive return on this investment" (p. 25).