Journal of Health Economics 38 (2014) 1–9

Contents lists available at ScienceDirect

Journal of Health Economics

journal homepage: www.elsevier.com/locate/econbase

Price regulation and relative delays in generic drug adoption

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ARTICLE INFO

Article history:
Received 26 June 2012
Received in revised form 29 March 2014
Accepted 2 April 2014
Available online 18 April 2014

JEL classification:
I11
I18
L1

Keywords:
Generic competition
Regulation
Adoption
Duration analysis

ABSTRACT

Increasing the adoption of generic drugs has the potential to improve static efficiency in a health system without harming pharmaceutical innovation. However, very little is known about the timing of generic adoption and diffusion. No prior study has empirically examined the differential launch times of generics across a comprehensive set of markets, or more specifically the delays in country specific adoption of generics relative to the first country of (generic) adoption. Drawing on data containing significant country and product variation across a lengthy time period (1999–2008), we use duration analysis to examine relative delays, across countries, in the adoption of generic drugs. Our results suggest that price regulation has a significant effect on reducing the time to launch of generics, with faster adoption in higher priced markets. The latter result is dependent on the degree of competition and the expected market size.

1. Introduction

Generic drugs are cheaper alternatives to branded medicines offering the most visible source of efficiency gain to any health system.[1] Understanding the determinants of generic drug launch is important, given such potential cost savings. Yet there is surprisingly scarce empirical evidence on the timing of first generic entry following patent expiry, or the reasons explaining launch delays across major pharmaceutical markets. Given the limited potential for product differentiation, generic producers predominantly engage in price competition, which can result in lower market share for branded products. Generic prices are markedly lower than branded products as innovation costs are negligible. The cost of bioavailability tests, to establish generic status, are significantly cheaper than the average R&D costs required for branded products to establish safety and clinical efficacy. It is estimated that this alone allows generic prices to be some 20–80% cheaper than originators (Simoens and de Coster, 2006). Griliches and Cockburn (1994) observed that branded market share falls by approximately 50% within two years of patent expiry due to the impact of generic competition. Berndt and Aitken (2010) state that the generics share in retail prescriptions in the USA had risen from under 20% in the mid-1980s to approximately 75% by 2009. In Europe, evidence suggests that the average prices of pharmaceutical products in Europe fall by approximately 20% during the first year of loss of (patent) exclusivity, and a further 5% over the next two years again as a result of generic competition (DG Competition, 2009). As branded prices tend to remain high initially after generic entry, the latter effect is attributable to lower generic prices. These lower prices can result in a high market share being obtained by generics. In the UK and Germany generic market share (in prescription units) is around 60% in aggregate, although this falls to under 40% in a number of other European countries; e.g. Austria, Belgium, Ireland, Portugal, and Spain (European Generics Association, 2009).

Of course, not all consumers perceive generic products as having the same quality as incumbent branded products. Brand loyal, price-insensitive consumers and physicians may be reluctant to switch from brand-name drug use (Frank and Salkever, 1992; Hellerstein, 1998; Coscelli, 2000). To counteract such behaviour, regulations are commonly put in place to promote generic substitution and market entry. For example, to avoid delays to generic entry once patent protection expires, Bolar exemptions or safe harbour provisions, were introduced in the US (with the Hatch Waxman Act in 1984) and the EU (with EC Directive 2004/28),

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[1] A generic drug is a chemically bioequivalent to any originator reference product with similar qualitative and quantitative composition in active ingredients, same form, route of administration, safety, and efficacy profiles (Scott Morton, 1999; Lichtenberg and Philipson, 2002).

http://dx.doi.org/10.1016/j.jhealeco.2014.04.004
0167-6296/

allowing generic manufacturers to conduct research and bioequivalence studies prior to protected branded product patent expiry in preparation for regulatory approval.[2]

Overall, the time it takes a generic drug from research lab to market can be as short as 3–5 years. Yet generic entry often takes longer than might be expected on the basis of patent expiry and the statutory loss of exclusivity of the originator product (DG Competition, 2009). If countries impose price and reimbursement regulation on such products, generic drugs can incur substantial delays to market entry, limiting patient access and delaying potential cost-savings to health insurers and, ultimately consumers. In the EU for example, despite attempts to support competitive practices through increasing market harmonisation, time delays for licensed generics were found to be an average of 6 months following patent expiry (Bongers and Carradinha, 2009; Hudson, 2000). If generic entry had taken place immediately upon loss of exclusivity over the period 2000–2007, savings arising from price competition within the EC would have been approximately €3 billion according to a DG Competition report, as based on an assumed slightly longer average delay of 7 months (DG Competition, 2009).

We argue in this paper, that the variation in the timing of first generic availability across countries can be explained by producers' ex ante price and sales volume expectations, which are themselves influenced by country-specific regulations and levels of competition. We analyse the (country) specific delay in the adoption of generic drugs by defining individual country launch relative to the first international (generic) launch for 20 major pharmaceutical markets over the period 1999–2008. This period which saw the introduction of substantial new regulatory changes in a number of the major Organisation of Economic Cooperation and Development (OECD) pharmaceuticals markets, including the harmonisation of EC pharmaceutical regulations in 2001 (EC Directive 2001/83/EC). Our empirical strategy uses duration analysis to estimate the impact of regulation on the probability of launch by incorporating local expected generic price information (proxying *de facto* regulation), controlling for market size, expected competition, type of molecule (active ingredient), and firm heterogeneity. This is the first study to provide an empirical analysis of launch-times for generics across a comprehensive set of major pharmaceutical markets.

The paper is structured as follows: Section 2 discusses the literature and sets the framework; Section 3 describes the data and the methodology used; Section 4 presents estimation results and finally Section 5 discusses findings and policy implications.

2. Previous literature and background

The literature has revealed a complex array of factors affecting generic market entry and adoption. Early empirical studies from the USA highlighted, amongst other factors, the importance of pre-entry market size and expected profits (Grabowski and Vernon, 1992; Scott Morton, 1999, 2000; Reiffen and Ward, 2005), firm and drug characteristics (Bae, 1997; Scott Morton, 1999), the loyalty attached to brand-name (Hurwitz and Caves, 1988; Hudson, 2000), and market structure and competition (Bae, 1997). However, the importance of each of these factors in determining entry dynamics differs strongly across therapeutic-classes (Saha et al., 2006).

Of the early studies, Bae (1997) explicitly investigated the speed of generic entry after patent expiry in the US market using a time duration model, finding that high market revenues experienced by branded drugs prior to patent expiry were associated with a higher probability of generic entry. The same study finds that a higher degree of competition in a therapeutic market, as proxied by the number of incumbent brand-name competitors, is correlated with slower generic penetration. Scott Morton (2000) finds that while increased numbers of brand-named competitors reduce generic penetration, increased numbers of generic products do not. Conversely, Saha et al. (2006) finds that generic market strategic deterrence is associated with the relative number of generic incumbents. A more recent study observes that the number of brand name competitors is associated with a positive impact on generic entry in a sample of several countries including the US, UK, Germany, and France (Magazzini et al., 2004).

There is also evidence that the probability of generic entry and the associated generated revenue are positively related (Frank and Salkever, 1997). Hudson (2000) identifies market size (proxied by original brand sales) at patent expiration to be the most significant determinant of generic entry in the US, the UK, Germany, and Japan. For Japan specifically, Iizuka (2009) finds that, consistent with the findings of Saha et al. (2006), higher numbers of competitors in the market discourage generic entry, although economies of scope in entering multiple markets and brand revenues are important determinants of generic entry. The evidence, whilst patchy, is then that expected competition has an impact, although the importance of this impact has not been fully established, while the related aspects of expected revenue and market size also appear important to generic launch strategy.

Several studies have also highlighted the role played by pharmaceutical price regulation on the development of the market for branded pharmaceutical products (e.g. Danzon and Chao, 2000b; Ekelund and Persson, 2003). The evidence on the impact of *different* regulatory practices on generic entry has, however, received limited empirical attention. Evidence from the Swedish market suggests that higher anticipated profits are associated with higher generic entry in this (price) regulated market (Rudholm, 2001). Recently a number of European markets have introduced reference pricing regulation for generic products, where the reference price is generally computed from the lowest priced generic product(s), which has expanded the adoption of generic products (see Kanavos et al., 2008). Yet, there is some evidence of generic entry deterrence in reference priced countries (Ekelund and Persson, 2003; Kanavos et al., 2008; Simoens and de Coster, 2006). Others have found that price regulation generally appears to be associated with reduced incentives for generic entry, and limited diffusion after entry (Danzon and Chao, 2000a; Garattini and Ghislandi, 2006; Simoens and de Coster, 2006).

Generic producers tend to pursue price competition strategies. Regulation of the generic market can augment this price competition by introducing various instruments (e.g. reference prices, lower cost sharing or higher pharmacist mark-ups for generic products) that attempt to lower prices for both branded and generic products after patent expiry. Given the potential loss in market share arising from generic entry, not surprisingly, innovator companies have developed several strategies to minimise this impact on the life-cycle profits of branded products, as documented by a number of studies (Appelt, 2009; Aronsson et al., 2001; Caves et al., 1991; Frank and Salkever, 1997; Grabowski and Vernon, 1992; Hollis, 2003; FTC, 2002a,b; Lexchin, 2006; Karwal, 2006; Magazzini et al., 2004; Suh et al., 1998; Wrowleski, 2002). Strategies include the combination of multiple patents into patent clusters, pursuit of litigation over the reformulation of the original molecule and expansion of patent protection. In some countries where direct to

[2] The adoption of similar regulations as the Bolar exemptions by Germany and the UK for example, has also meant that generic medicines can obtain immediate price and reimbursement approval from health insurance authorities following market authorisation in those countries. The passage of the Patent Protection and Affordable Care Act (2010) in the USA is likely to further ease market entry for generics in this major market (Berndt and Aitken, 2010).