

Preliminary Injunctions in Pharmaceutical Litigation

The Economics of Irreparable Harm

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Contents

Introduction

Section 1: Initial Impact of Generic
Entry on Branded Drug Company
Revenues.....2

Section 2: Irreparable Harm Arising
from "At Risk" Generic Entry.....4

Section 3: Preliminary Injunction De-
cisions.....7

Conclusion

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Introduction

A plaintiff who seeks to obtain a preliminary injunction must establish:

- (i) *that success on the merits of its claims is reasonably likely;*
- (ii) *that proceeding without the injunction will cause irreparable harm to the company;*
- (iii) *that the balance of hardships weighs in its favor; and*
- (iv) *that the injunction will have a favorable impact on the public interest.¹*

The law defines irreparable harm as harm that cannot be undone or compensated for with monetary damages.² While economists can estimate the monetary damages associated with virtually any harm, some types of harm are much more difficult to quantify with precision than others. Harms that are especially difficult to quantify with precision have been regarded by the courts as irreparable.³

According to some observers, recent court decisions such as *eBay*⁴ and *Winter*⁵ have raised the standards for obtaining injunctive relief. In particular, a number of legal scholars have argued that irreparable harm can no longer be presumed from a plaintiff's demonstration that it will likely succeed on the merits of its claims.⁶ Given an increased need to demonstrate irreparable harm as an independent factor in a preliminary injunction case, this paper focuses on the economic arguments that can be used to demonstrate irreparable harm in one particular context: "at risk" launch by a generic drug maker.

"At risk" launches can occur when a generic drug maker challenges the extant patent(s) on a particular branded drug under Paragraph IV of the Hatch-Waxman Act.⁷ If the patent holder on the branded drug files a patent infringement suit within 45 days of the Paragraph IV challenge, this filing will prevent the generic from launching for the next 30 months. If, by the end of the 30-month stay, the suit against the generic drug company still has not been resolved, the generic drug company has the option to launch "at risk."⁸

Preliminary Injunctions in Pharmaceutical Litigation

If the generic drug maker does choose to launch “at risk”, the branded drug company may seek a preliminary injunction to prevent this launch. In light of the *eBay* and *Winter* decisions, branded drug company plaintiffs may need to develop stronger arguments than were previously required in order to demonstrate irreparable harm.

This paper discusses the sources of harm that courts have accepted as being irreparable in prior decisions, including reductions in funds for research and development (R&D), loss of share to therapeutic competitors, loss of goodwill, and negative effects on employment and manufacturing facilities.⁹ Section 1 explains the initial effect of generic entry on revenues and sales volumes of the branded drug company. This discussion sets the stage for Section 2, which describes the irreparable harm that can ensue from lost sales, as well as other forms of irreparable harm that can arise from “at risk” generic entry. Section 3 discusses court decisions that have upheld plaintiffs’ claims for preliminary injunctions to prevent “at risk” generic entry, with a focus on how courts have responded to branded drug company claims of irreparable harm.

Section 1 INITIAL IMPACT OF GENERIC ENTRY ON BRANDED DRUG COMPANY REVENUES

In general, the introduction of a lower-priced generic equivalent to a branded drug will result in a rapid and severe loss in revenues for the branded drug. The factors that drive this dramatic revenue erosion depend to some extent on whether the drug at issue is dispensed by pharmacists or whether it is one of a much smaller set of specialty drugs that are typically administered by physicians in private practice or in hospitals. The factors driving revenue losses for each type of drug are discussed below. These revenue losses in and of themselves may be amenable to reasonably precise quantification and therefore monetary damages could compensate for them. However, such lost revenues can produce effects that are difficult to measure with precision and therefore satisfy the legal criteria for irreparable harm, as detailed in the next section.

1.1 DRUGS DISPENSED BY PHARMACISTS

For drugs that are dispensed by pharmacists, there are three sets of actors with incentives to purchase generics rather than branded versions. First, patients without insurance coverage for the drug at issue, as well as patients who face coinsurance payments for their drug purchases, have incentives to purchase generics because such drugs typically cost at least 25 percent less than the branded version of the drug.¹⁰ Second, pharmacists have strong financial incentives to switch patients to the generic version because they generally earn higher margins on the sale of generic drugs than on branded versions.¹¹ In most states, pharmacists may substitute a generic drug for a branded drug without consulting the patient and doctor, unless a doctor has indicated in writing on the prescription that it must be dispensed as written.¹² Finally, many drug purchasers have incentives to purchase generics due to the behavior of third party payers (TPPs) such as Medicare Part D, private insurers, and/or pharmacy benefit managers (PBMs).¹³ These TPPs encourage generic purchases by charging lower copayments for generic as opposed to branded purchases, as discussed in Section 2.¹⁴

Given these financial incentives, it is not surprising that several academic studies have shown that branded drugs typically lose over 75 percent of their prescriptions in the three months following generic entry, and over 80 percent in the six months after generic entry.¹⁵ In fact, some evidence suggests that the loss of prescriptions to generics has further increased since those studies were performed. For example, Pravachol® and Zoloft®, which faced generic entry in April and August 2006 respectively, lost approximately 80 percent of their prescriptions to generics within three weeks of generic entry.¹⁶ Similarly, Allegra®, which faced generic entry in September 2005, lost approximately 80 percent of its prescriptions to the generic after just five weeks.¹⁷ This loss in branded prescriptions leads to a loss in revenues for the branded drug company.¹⁸

Preliminary Injunctions in Pharmaceutical Litigation

Of course, the branded drug company could attempt to stem losses in prescriptions by reducing the price of its product.¹⁹ However, even if a branded drug company lowers its price in order to retain prescriptions, it will still lose revenue. With revenue equal to prescriptions multiplied by price, generic entry will have a negative impact on a branded drug company's revenues, regardless of whether the branded drug company seeks to maintain pre-entry prices or prescription volume.

1.2 SPECIALTY DRUGS DISPENSED BY PHYSICIANS AND/OR HOSPITALS

Public and private insurers, which typically cover most if not all of the cost of chemotherapy and other specialty drugs, also employ a variety of strategies to drive physician and hospital purchasers of these specialty drugs towards generics. One of the most important of these strategies is reimbursement policy. Under Medicare Part B, the Medicare drug benefit that applies to chemotherapy and other specialty drugs, the purchaser receives a fixed reimbursement regardless of whether a generic or branded drug was purchased.²⁰ This amount is 106 percent of the volume-weighted average sales price (ASP) for the drug molecule (which encompasses both the branded drug and its generic equivalent).²¹ Private health care plans use similar models to provide physicians with an incentive to reduce drug purchase costs,²² although such plans often provide physicians who prescribe oncology drugs with much higher mark-ups than Medicare's six percent.²³

Since these rules reimburse purchasers with the same fixed dollar amount for the branded drug and its generic equivalent, purchasers have a strong incentive to choose the cheaper generic. Under Medicare Part B, this incentive is particularly strong at the time of generic entry because the volume-weighted ASP reimbursement amount is set with a two-quarter lag.²⁴ Hence, in the first two quarters of generic entry, Medicare reimburses physicians for the cost of branded drugs, regardless of whether the physicians are purchasing branded or generic drugs for their patients. As a result, physicians have a strong incentive to purchase the lower-priced generic and receive reimbursement at the higher branded drug price in those first two quarters. In later quarters, this system continues to positively reward physicians for prescribing the generic. However, the positive reward declines over time, as the share of drug molecule sales attributable to the lower-priced generic increases (albeit, on a lagged basis).²⁵



Section 2 IRREPARABLE HARM ARISING FROM “AT RISK” GENERIC ENTRY

As discussed in Section 1, “at risk” generic entry can be expected to dramatically reduce revenues for the branded drug, regardless of whether it is dispensed by pharmacists or administered by physicians. Overall, however, revenue reductions can usually be quantified with reasonable precision. However, “at risk” generic entry can also lead to several forms of harm that are more difficult to quantify and that therefore satisfy the legal criteria for irreparable harm.

2.1 REDUCTIONS IN OVERALL R&D BUDGETS

Economic analysis indicates that forgone investment in R&D is an important source of irreparable harm arising from “at risk” generic entry. Generic entry can be expected to result in immediate and dramatic revenue losses to a branded drug company, and these revenue reductions will typically reduce the branded drug company’s R&D budget. This is because branded drug companies tend to fund R&D with internal financing sources, as opposed to external financing sources such as debt and equity.

Pharmaceutical firms typically do not fund their R&D investments with debt for a number of reasons. First, when a pharmaceutical firm initiates an R&D project, it takes on significant obligations in the form of future capital outlays required to bring the drug to the production and marketing stage. These R&D funding obligations are similar to debt obligations because they increase the firm’s riskiness, and hence its cost of capital. As a result, funding R&D through additional debt can often be prohibitively expensive for the firm.²⁶ In addition, bankers and other debt holders are often reluctant to lend when a project involves substantial R&D investment because they prefer to use physical assets like plant and equipment as collateral for loans.²⁷

Pharmaceutical firms can also face difficulty in financing their R&D investments with equity because of the well-known “lemons problem” in economics. When potential investors are less informed than management about the probability that a firm’s R&D investment will be a success, the investors may demand a discount on equity shares in order to mitigate their risk of investing in a “lemon.” However, the need to discount will discourage firms whose investments are not lemons from issuing equity. With neither debt nor equity available to finance R&D projects at reasonable cost, firms will have no choice but to finance their R&D investments with retained earnings.²⁸ In fact, research has shown that internal financing sources such as cash flows and expected returns on R&D are important determinants of pharmaceutical firms’ “research intensities.”²⁹ According to one study, R&D investment decreases by about twenty-two cents with every dollar reduction in cash flow.³⁰

It is difficult to precisely quantify the impact of forgone R&D on either a branded drug company or on the patients who could have benefitted from the findings of this research. This quantification issue arises in large part because the drug development process is lengthy, risky, and highly uncertain. In fact, the U.S. Food and Drug Administration (FDA) estimates that “[n]o more than 5 in 5,000 tested compounds pass ... preclinical trials and are proposed for clinical studies.”³¹ Moreover, more than three-quarters of all drugs that enter clinical testing ultimately fail to receive marketing approval in the United States. Even for drugs that receive such marketing approval, the process is lengthy. The average approved drug takes over seven years to travel from clinical trials to marketing approval by the FDA.³²

It is important to note that curtailed or cancelled research projects can also irreparably harm a branded drug company that is engaged in an R&D “race.” This is because the U.S. patent system provides all rewards associated with an innovation to the first inventor. As a result, a branded drug company that falls behind rivals in researching a drug that subsequently turns out to be successful in an R&D race stands to forego significant — but highly uncertain — profits.³³

2.2 BRANDED DRUG COMPANY CURTAILMENTS IN DRUG-SPECIFIC R&D AND MARKETING INVESTMENTS

Following “at risk” generic entry, a branded drug company has a greatly reduced incentive to pursue R&D that is specific to the branded drug at issue. This is because any prescriptions generated by the results of this R&D are likely to be filled by the cheaper generic drug. With the generic entrant able to “free ride” off the branded drug company’s R&D investments in this way, the branded drug company will often delay and/or curtail R&D efforts specific to that drug. In so doing, however, the branded drug company may miss potentially valuable commercial opportunities associated with the development of new indications for the drug at issue.³⁴

These same “free rider” issues also provide the branded drug company with a strong incentive to reduce promotional expenditures for its product following “at risk” generic entry. Again, any additional prescriptions generated by these promotional efforts are likely to be filled by the cheaper generic drug.³⁵ Thus, if a branded drug that is subject to generic challenge has recently been approved by the FDA for use in a new indication, reduced promotional expenditures can prevent physicians and patients from learning about a potentially helpful new therapeutic alternative. Economic logic indicates that it can be difficult to precisely estimate how physicians and patients would have behaved had they known about the drug’s new indication. As a result, the branded drug company’s lost sales can satisfy the legal criteria for irreparability.

Even in the absence of a new indication, curtailed or reduced promotions following generic entry can irreparably harm the branded drug company. This is because promotion is an important means through which companies with branded drugs in the same therapeutic category compete with one another. With reduced promotional support, the branded drug can often expect to lose sales to branded therapeutic competitors, as well as to the generic entrant. However, measuring the harm that the branded drug suffers due to diminished promotions can be very difficult; it would require quantifying sales that the branded drug lost to each rival branded drug (including new entrants). It would also require quantifying sales lost to the generic entrant in a market that is evolving over time. When the branded drug company’s lost sales are extremely difficult to quantify with precision, this harm can also satisfy the legal criteria for irreparability.³⁶

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2.3 FORMULARY DISPLACEMENT

Formularies are lists of drugs compiled by TPPs that establish the copayments for prescription drugs dispensed by pharmacists. Formularies often have three tiers: Tier 1 is typically reserved for generic drugs, Tier 2 for preferred branded drugs, and Tier 3 for non-preferred branded drugs. In tiered formularies, the higher the tier, the less favorable — i.e., the more expensive — the copayment. Thus, generic drugs usually have the lowest copayments, preferred branded drugs have intermediate copayments, and non-preferred branded drugs have the highest copayments.³⁷

With higher copayments associated with higher formula tiers, a drug's position in the formulary tier structure has an important effect on the demand for a particular prescription. Because of the relatively favorable copayment associated with Tier 2, branded drugs seek to maintain this status on formularies. With several branded drugs treating the same therapeutic conditions (as in the case of antidepressants or ulcer medications), the competition among branded drugs to obtain and maintain Tier 2 status can be intense. Further, an "at risk" launch can have a significant effect on this competitive situation.

When a TPP can provide a generic version of the branded drug at issue on its formulary, the TPP will have less reason to maintain the branded version of that same drug on Tier 2. Aware of TPP incentives, branded competitors often intensify their efforts to displace the challenged drug on those formularies where it has Tier 2 status. Displacement efforts by branded rivals typically take the form of offering increased rebates and product discounts to relevant TPPs. TPPs may also unilaterally decide to replace the challenged drug with another branded product as the Tier 2 drug, moving the challenged drug to a higher tier or off the formulary entirely.³⁸

When a branded drug loses its Tier 2 status, its subsequent restoration to Tier 2 in the event of generic withdrawal is highly uncertain. This is because the economic conditions that prevailed when the branded drug was originally placed on Tier 2 may no longer exist by the time the generic is withdrawn. For example, if new or current branded competitors have taken over the Tier 2 formulary position, negotiations to restore the branded drug to its former Tier 2 status can be more difficult. Economic analysis therefore suggests that the harm arising from formulary displacement can be difficult to quantify, thereby satisfying the legal criteria for irreparability.³⁹

2.4 LOST GOODWILL

Generic entry can also cause the branded drug at issue to suffer a loss in patient goodwill, even if the company prevails in its patent infringement suit. This is because payers who purchased the generic prior to its withdrawal will now have to pay more for the same drug because the generic is no longer available. These losses in patient goodwill and sales are typically very difficult to quantify, making them another potential source of irreparable harm arising from generic entry.

In the case of drugs dispensed by pharmacists, insured patients are likely to face higher copayments once the generic is withdrawn. As a result, when the branded drug's generic equivalent is no longer available, patients who had been using that generic equivalent may switch to using the generic versions of other drugs in the same therapeutic category, rather than the branded drug, in order to maintain low copayments.⁴⁰

In the case of physician-administered or specialty drugs, there is also a significant prospect of lost payer goodwill. This is because the Medicare Part B reimbursement plan that often applies to such drugs will produce reimbursement prices that are close to generic levels once the generic has been available to consumers for six to nine months. Thus, if the price of the branded specialty drug were greater than the Medicare Part B reimbursement price at the time the generic is withdrawn, providers who purchased the branded drug would suffer a loss; their reimbursements would be substantially less than the drug's price.

Preliminary Injunctions in Pharmaceutical Litigation

Not surprisingly, physicians (and branded drug companies) would prefer to avoid this situation, which is referred to as being “under water.” Because losses in patient and physician goodwill are intangible in nature, and because the switching of former patients from the branded drug to generic products can be difficult to quantify with precision, both effects may satisfy the legal criteria for irreparability.

2.5 OTHER SOURCES OF IRREPARABLE HARM

“At risk” generic entry can also irreparably harm the branded drug company by causing the company to lay off employees and close facilities. First, reductions in the branded drug company’s R&D budget, as well as the curtailment or abandonment of planned research related to the patented drug, could spur an exodus of talent from the company. If the branded drug company has fewer products and clinical trials to design and run, research scientists and clinicians might seek employment at other companies, including competitors, in order to stay active in their specialty area. As a result, the branded drug company could suffer a long-term negative impact. That negative impact could be extremely difficult to estimate with precision and could therefore satisfy the legal criteria for irreparability.⁴¹

The launch of a generic drug could also lead the branded drug company to scale back its manufacturing operations and lay off employees in manufacturing, packaging, marketing, and quality control. For example, Wyeth, which faced unexpected generic competition for both Protonix® and Effexor® in late 2007 and early 2008, announced 5,000 job cuts in January 2008.⁴² Similarly, the unexpected launch of a generic version of OxyContin® resulted in a loss of more than 1,800 jobs at Purdue Pharma.⁴³ The negative impact of these layoffs on the branded drug company itself, as well as its employees, may be difficult to quantify with precision and therefore may also satisfy the legal criteria for irreparability.



Section 3 PRELIMINARY INJUNCTION DECISIONS

Below is a review of irreparable harm findings in six cases in which district courts granted a preliminary injunction to the branded drug company, and a description of the support offered for claims of irreparable harm. Although the majority of these decisions pre-date *Winter*, they exemplify the many types of injuries that the courts have accepted as evidence of irreparable harm. This list is not intended to be exhaustive but merely illustrative of court findings in which plaintiffs have prevailed in their claims.

Pharmacia & Upjohn Co. v. Ranbaxy Pharmaceuticals Inc. (Vantin®)

In December 2000, Ranbaxy filed two Abbreviated New Drug Applications (ANDAs) with the FDA, seeking approval to market generic versions of Vantin®, a drug used to treat bacterial infections.⁴⁴ The FDA approved Ranbaxy’s application to market its oral suspension formulation. Meanwhile, Pharmacia filed a motion for preliminary injunction, seeking to prevent Ranbaxy from infringing its patents associated with Vantin®. This motion was granted on July 18, 2003. In its decision, the district court concluded that Pharmacia & Upjohn had made the requisite strong showing for a presumption of irreparable harm to apply.

Preliminary Injunctions in Pharmaceutical Litigation

In addition, it opined that this finding of irreparable harm was further supported by the relatively short remaining life of the patent at issue, the irretrievable price and market erosion for the patented product, loss of current research opportunities resulting from loss of funding, and the speculative nature of damage assessments and difficulty of pursuing award collection in international legal systems.⁴⁵ This finding was upheld on appeal.⁴⁶

Eisai v. Teva (Aricept®)

In October 2005, Teva filed an ANDA seeking approval to market a generic version of Eisai's drug for Alzheimer's disease, Aricept®. This ANDA included a Paragraph IV certification, which attacked Eisai's patent as being invalid and unenforceable. In December 2005, Eisai sued Teva for infringing patents associated with Aricept®, thereby triggering a 30-month stay on the FDA's approval of Teva's generic product. With this 30-month stay expiring in April 2008, Eisai sought a preliminary injunction to prevent Teva from marketing "at risk" a generic version of Aricept®.

The district court granted Eisai's motion for a preliminary injunction against Teva. In its decision, the court opined that Eisai was entitled to a presumption of irreparable harm because the would-be generic entrant, Teva, stipulated to infringement and validity, and Eisai demonstrated a likelihood of success on the question of enforceability. Regardless of the presumption, however, the court found that Eisai had independently demonstrated actual irreparable harm. In particular, the court noted that U.S. sales of Aricept® accounted for 70 percent of Eisai's U.S. subsidiary's profits and 25 percent of Eisai's revenues worldwide.

Given the volume of sales, the court agreed with Eisai's economic expert that R&D projects dependent on Aricept® profits for continued viability would be in danger of being short-circuited or shut down altogether in the event of an "at risk" generic launch. The court also stated that such harm could not be readily compensated with monetary damages as long as there was a reasonable likelihood that research on future drugs might be eliminated, or even reduced or delayed.⁴⁷

Eli Lilly and Company v. Teva (Evista®)

In early 2006, Teva filed an ANDA with the FDA, seeking approval to manufacture and market a generic version of Lilly's osteoporosis drug, Evista®, along with Paragraph IV certifications. In June 2006, Lilly sued Teva for infringing patents associated with Evista®, thereby triggering a 30-month stay on the FDA's approval of Teva's generic product. This stay, which was originally set to expire in November 2008, was later extended for several months. On April 22, 2009, the district court approved Lilly's motion for a preliminary injunction to prevent Teva from launching a generic version of Evista® "at risk".

The district court found that Lilly's loss of marketing exclusivity with respect to Evista® would result in a rapid loss of market share and revenue that would be difficult, if not impossible, for Lilly to recover, given the issues associated with the recovery of its preferred status on formularies. The district court also found that even if Lilly were able to fully recover its position in the market, it would nonetheless suffer irreparable damage to its relationship with physicians and customers. Finally, the court found that an injunction was warranted to prevent significantly disrupting research that otherwise would have been sponsored or completed by Lilly.⁴⁸

Sanofi-Synthelabo, Inc. and Bristol-Myers Squibb Sanofi Pharmaceuticals Holding Partnership v. Apotex Corp. (Plavix®)

In November 2001, Apotex filed an ANDA seeking FDA approval to manufacture and sell a generic version of Plavix®, as well as a Paragraph IV certification asserting that Sanofi's patent was invalid. In response, Sanofi sued Apotex on March 2002, claiming that the filing of the ANDA infringed one of its patents and triggering a 30-month stay on Apotex' generic launch. After the expiration of the 30-month stay, Apotex launched its generic version of Plavix® "at risk." Five business days after the launch, Sanofi moved for a preliminary injunction to terminate these sales; the district court granted Sanofi's request two weeks later, on August 31, 2006.

Preliminary Injunctions in Pharmaceutical Litigation

In its decision approving the injunction, the district court found that Sanofi had clearly established a likelihood of success on the merits of its claims and should therefore receive the benefit of a presumption of irreparable harm. In addition, it found that Sanofi had provided independent evidence of irreparable harm arising from several adverse effects of “at risk” generic entry, including irreversible price erosion associated with formulary displacement and loss of goodwill from customers who would become accustomed to lower generic prices. Other effects cited by the district court included layoffs of employees involved in marketing Plavix® and the potential suspension of clinical trials for new applications for Plavix®.⁴⁹ This decision was upheld on appeal.⁵⁰

The Purdue Pharma Company v. Roxane Laboratories, Inc., Boehringer Ingelheim Corporation (OxyContin®)

The two branded pharmaceutical companies in this matter, Purdue and Roxane, had each developed controlled-release oxycodone medications for treating pain. On May 18, 1999, Purdue filed suit against Roxane alleging that its oxycodone controlled-release product infringed claims in three of Purdue’s patents.

In May 2000, the district court granted Purdue’s request for a preliminary injunction, finding that Purdue had clearly established a likelihood of success on the merits and should therefore receive the benefit of a presumption of irreparable harm. In addition, it found that Purdue had provided supportive evidence of irreparable harm from (a) future effects of price erosion, (b) loss of experienced staff resulting from cuts required by the loss of revenue, (c) disruption to Purdue’s sales force from having to respond to the introduction of the generic at issue, and (d) lost allocation of revenues to further R&D, together with the consequent lost future opportunities in the marketplace. The finding in favor of Purdue was upheld on appeal.⁵¹

Abbott Laboratories v. Sandoz, Inc. (Biaxin XL®)

This suit concerned two Abbott Laboratories patents on extended release formulations of the antibiotic drug clarithromycin, sold by Abbott under the brand name Biaxin XL®. In April 2007, Abbott sought a preliminary injunction to prevent Sandoz from launching a generic version of Biaxin XL®.

In its decision granting Abbott the injunction, the district court found that Abbott was entitled to a presumption of irreparable harm. Further, it found that Sandoz did not rebut the presumption of harm with its arguments against Abbott’s contentions that it would lose market share, profits, and goodwill and that it would be constrained to lay off several hundred sales representatives.⁵² The court of appeals upheld the district court’s finding that these sources of losses constituted irreparable harm to Abbott.⁵³

Conclusion

According to some industry observers, the standards for obtaining a preliminary injunction have been raised due to the *eBay* and *Winter* decisions. Consequently, the irreparable harm portion of the four-pronged test for a preliminary injunction can no longer merely be presumed based on a strong showing of the likelihood of success on the merits of the claims.

Given an increased need to demonstrate irreparable harm as an independent factor in a preliminary injunction case, it is important to consider the economic arguments that can be used by branded drug companies to demonstrate that irreparable harm can result from a generic drug maker’s “at risk” launch. “At risk” generic launches can cause unquantifiable damage to branded drug companies’ ability to retain R&D funds, market share, customer goodwill, employment, and manufacturing facilities. Previous court decisions have recognized all of the foregoing as harms, providing potential avenues for branded drug company plaintiffs to make a persuasive legal case when confronted with an “at risk” generic launch.

Endnotes

¹ *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1350 (Fed. Cir. 2001). The balance of hardship test focuses on whether the patent holder will lose more from the claimed infringement than an accused infringer will gain. The public interest standard focuses on whether there is some critical public interest that would be injured by the grant of preliminary relief, given the public interest in competition.

² According to the U.S. Court of Appeals for the Federal Circuit, “[t]he nature of the patent grant [thus] weighs against holding that monetary damages will always suffice to make the patentee whole, for the principal value of a patent is its statutory right to exclude.” See *H.H. Robertson Co. v. United Steel Deck Inc.*, 820 F.2d 384, 390 (Fed. Cir. 1987). Similarly, in *Hybritech Incorporated v. Abbott Laboratories*, 849 F.2d 1446 (Fed. Cir. 1988), the Court of Appeals states “[t]he patent statute provides injunctive relief to preserve the legal interests of the parties against future infringement which may have market effects never fully compensable in money.”

³ See *Allied Marketing Group, Inc. v. CDL Marketing, Inc.*, 878 F.2d 806, 810 n.1 (5th Cir. 1989): recognizing irreparable harm where “economic rights are involved when the nature of those rights makes establishment of the dollar value of the loss ... especially difficult or speculative”; and *Reebok International Ltd v. J. Baker, Inc.*, 32 F.3d 1552, 1558 (U.S. Court of Appeals, August 15, 1994): “Harm to reputation resulting from confusion between an inferior accused product and a patentee’s superior product is a type of harm that is not fully compensable by money because the damages caused are speculative and difficult to measure.”

⁴ *eBay Inc. v. Mercantile Exchange, LLC*, 547 U.S. 388, 2391 (2006) (hereinafter “eBay”).

⁵ *Winter v. Natural Resources Defense Council*, 129 S. Ct. 365, 375-76 (2008) (hereinafter “Winter”).

⁶ See Samuelson and Bebenek, “Why Plaintiffs Should Have to Prove Irreparable Harm in Copyright Preliminary Injunction Cases,” *I/S: Journal of Law and Policy for the Information Society*, 2009. According to these authors: “[Winter] thus makes it obvious that courts should not presume irreparable harm merely because a copyright owner or a patent owner has proven a likelihood of success on the merits.”

⁷ The Hatch-Waxman Act, passed by Congress in 1984, comprised a series of amendments to the Federal Food, Drug, and Cosmetic Act (FDCA) and the Patent Act (21 U.S.C. §355 (2006)); 35 U.S.C. §271 (2006). It effectively lowered the barriers and raised the incentives for market entry by manufacturers of generic drugs.

⁸ See Perchersky, “To Achieve Closure of the Hatch-Waxman Act’s Loopholes, Legislative Action is Unnecessary: Generic Manufacturers Are Able to Hold Their Own,” *Cardozo Arts and Entertainment Law Journal*, 2007.

⁹ These sources of harm have not been accepted as irreparable in all prior decisions reviewed.

¹⁰ Saha, Grabowski, et al., “Generic Competition in the US Pharmaceutical Industry,” *International Journal of the Economics of Business*, February 2006. Note that coinsurance requires the insured to assume a percentage of the cost of covered services. In contrast, copayments require the insured to pay a flat fee for covered services, e.g., \$5 per prescription drug. Unlike coinsurance, copayments do not vary with the cost of service.

¹¹ *Ibid.*

¹² National Association of Boards of Pharmacy, Survey of Pharmacy Law, 2006.

¹³ PBMs are firms that provide oversight of prescription drug plans for employers and managed care organizations.

¹⁴ Richardson, The Health Strategies Consultancy, “PBMs: The Basics and an Industry Overview,” presentation, June 26, 2003. Available at: <http://www.ftc.gov/ogc/healthcarehearings/docs/03026richardson.pdf>.

¹⁵ Grabowski, “Are the Economics of Pharmaceutical Research and Development Changing? Productivity, Patents and Political Pressures,” *Pharmacoeconomics*, 2004. See also Hudson, “Generic take-up in the pharmaceutical market following patent expiry: a multi-country study,” *International Review of Law and Economics*, 2000, and Saha, Grabowski, et al., “Generic Competition in the US Pharmaceutical Industry,” *International Journal of the Economics of Business*, February 2006.

¹⁶ Silver, “A Wall Street Perspective on Generics,” 2007 GPhA Annual Meeting, Phoenix, AZ, March 1-3, 2007.

¹⁷ *Ibid.*

¹⁸ Although these are not examples of “at risk” generic entry, they do illustrate the fact that generic launches cause the pioneer company to lose a significant share of its revenues.

¹⁹ Price is defined here as net of rebates offered to TPPs.

²⁰ Medicare Part B drug coverage applies in the following circumstances: 1. Drugs billed by physicians and provided incident to physician service for that patient (e.g., chemotherapy drugs). 2. Drugs billed by pharmacy suppliers and administered through durable medical equipment (DME) benefit (e.g., respiratory drugs given via nebulizer). 3. Some drugs billed by pharmacy suppliers and self-administered by the patient (e.g., immunosuppressive drugs, some oral anti-cancer drugs). 4. Separately billable drugs

Preliminary Injunctions in Pharmaceutical Litigation

provided in hospital outpatient departments. Increasingly, Medicare is bundling drug costs within outpatient hospital payment rates. 5. Separately billable End Stage Renal Disease (ESRD) drugs (e.g., erythropoietin). Increasingly, Medicare is bundling ESRD drug costs within ESRD facility payment rates. See www.healthlaw.org/library/attachment.82007 and Foley & Lardner LLP, "Pharmaceutical Manufactures Now Required to Report Average Sales Price Data," *Law Watch*, 2004.

²¹ ASP is defined by statute "as a manufacturer's sales of a drug to all purchasers in the United States in a calendar quarter divided by the total number of units of the drug sold by the manufacturer in that same quarter. The ASP is net of any price concessions such as volume discounts, prompt pay discounts, and cash discounts; free goods contingent on purchase requirements; chargebacks; and rebates other than those obtained through the Medicaid drug rebate program." See Daniel R. Levinson, Inspector General, "Monitoring Medicare Part B Drug Prices: A Comparison of Average Sales Price to Average Manufacturer Prices," Department of Health and Human Services, OEI-03-04-00430, April 2006. As noted in this source, the Medicare Part B reimbursement methodology took effect in 2005.

²² Mullen, "The Arrival of Average Sales Price," *Biology Healthcare*, June 2007. See also Mullins, et al., "Health Plans' Strategies for Managing Outpatient Specialty Pharmaceuticals," *Health Affairs*, 2006.

²³ *Ibid.*

²⁴ Medicare Payment Advisory Commission, "Impact of Changes in Medicare Payments for Part B Drugs," January 2007. Available at: http://www.medpac.gov/documents/jan07_partb_mandated_report.pdf.

²⁵ By definition, no generic sales would be possible in the quarter prior to generic entry. See Medicare Payment Advisory Commission, "Impact of Changes in Medicare Payments for Part B Drugs," January 2007. Available at: http://www.medpac.gov/documents/jan07_partb_mandated_report.pdf. "The ASP payment rate is based on these transaction prices from two quarters prior. Thus, if manufacturers raise prices in the succeeding quarters, purchasers may have difficulty purchasing products at the Medicare payment rate until the ASP 'catches up.' On the other hand, if prices go down, either because of competition between therapeutically equivalent branded drugs or because a generic version of a branded drug becomes available, purchasers may buy products at prices significantly below the payment rate until the ASP catches up."

²⁶ See Myers and Howe, "A Life-Cycle Financial Model of Pharmaceutical R&D," Working Paper, Program on the Pharmaceutical Industry, Massachusetts Institute of Technology, Cambridge, MA, April 1997, and Myers and Shyam-Sunder, "Measuring Pharmaceutical Industry Risk and the Cost of Capital," in Helms, ed., *Competitive Strategies in the Pharmaceutical Industry* (Washington, DC: American Enterprise Institute, 1996).

²⁷ See Hall, "The Financing of Research and Development," *Oxford Review of Economics Policy*, 2002 at p. 38 and references cited therein.

²⁸ Myers and Majluf, "Corporate Financing and Investment Decisions When Firms Have Information that Investors Do Not Have," *Journal of Financial Economics*, 1984.

²⁹ Grabowski and Vernon, "The Determinants of Pharmaceutical Research and Development Expenditures," *Journal of Evolutionary Economics*, 2000.

³⁰ Vernon, "Pharmaceutical R&D Investment and Cash Flows: An Instrumental Variables Approach to Testing for Capital Market Imperfections," *Journal of Pharmaceutical Finance, Economics and Policy*, 2004.

³¹ U.S. Food and Drug Administration, "FDA and the Drug Development Process: How the Agency Ensures That Drugs are Safe and Effective," Publication No. FS 02-5, February 2002. Available at: <http://www.fda.gov/opacom/factsheets/justthefacts/17drgdev.pdf>.

³² DiMasi, Hansen, and Grabowski, "The price of innovation: new estimates of drug development costs," *Journal of Health Economics*, 2003.

³³ Robinson, et al., "First-Mover Advantages from Pioneering New Markets: A Survey of Empirical Evidence," *Review of Industrial Organization*, 1994; and Cockburn and Henderson, "Racing to Invest? The Dynamics of Competition in Ethical Drug Discovery," *Journal of Economics and Management Strategy*, 1994.

³⁴ Generic drug companies compete by providing customers with inexpensive bio-equivalent versions of existing drugs; they do not typically engage in research in support of their generic products. Hence, if the branded drug company curtails R&D on new indications for a product subject to generic challenge, the generic company cannot be expected to offset this reduction with R&D support of the generic. This reduced drug-specific R&D can also be expected to harm the public interest by depriving patients of the benefits of research on new indications.

³⁵ Because pharmacies can substitute generic drugs for branded drugs without physician authorization, generics typically compete on the prices charged to pharmacies and wholesalers rather than through promotions to physicians and patients. In contrast, branded drug companies rely heavily on promotion to physicians and patients, both to provide new information on drug benefits and to remind them of existing features. See Leffler, "Persuasion or Information? The Economics of Prescription Drug Advertising," *Journal of Law and Economics*, 1981.

³⁶ Similarly, it can be difficult to quantify the benefits that patients would have received if their physicians had prescribed the new treatment option. As noted previously, this harm to patients can be useful in establishing the public interest prong of the four-part test for a preliminary injunction.

Preliminary Injunctions in Pharmaceutical Litigation

³⁷ Richardson, The Health Strategies Consultancy, "PBMs: The Basics and an Industry Overview," presentation, June 26, 2003 at p. 20. Available at: <http://www.ftc.gov/ogc/healthcarehearings/docs/03026richardson.pdf>.

³⁸ Some formularies may reserve Tier 2 only for branded drugs that do not have generic equivalents. See U.S. Federal Trade Commission Staff Comment to Terry G. Kilgore, October 2, 2006 at p.4, footnote 17. Available at: <http://www.ftc.gov/be/V060018.pdf>.

³⁹ Of course, the branded drug company could reduce its price to TPPs in order to mitigate this loss of formulary position; such reductions are typically offered in the form of rebates and discounts. However, the ability of branded drugs to regain price concessions after the withdrawal of the generic is also unknown and highly uncertain. Thus, the price erosion caused by at risk generic entry could continue after the issuance of an injunction, and the resulting damages may be difficult to ascertain and thus irreparable.

⁴⁰ Academic research has shown that consumers perceive a loss or gain based on the difference between actual price paid and his or her reference price, where the reference price could reflect either the last price paid by the consumer or the consumer's expectation of the product price. Consumers who reap the gain of reduced copayments for a generic could subsequently perceive a loss after the departure of the generic, due to increased copayments. There is significant academic literature indicating that consumers assign greater weight to a loss (due to price increase) than to a gain of the same magnitude. (See, Kahneman, and Tversky, "Prospect Theory: An Analysis of Decision Under Risk," *Econometrica*, 1979). Hence, the change in copayments can lead to a loss of goodwill.

⁴¹ It is also important to note that branded drug companies often budget discretionary funds to educational grants, patient assistance programs, and other activities that could be imperiled by "at risk" generic entry. Faced with a significant reduction in its revenues, the branded drug company would have strong incentives to cut these and other discretionary expenditures. Such cuts would have an adverse impact on the branded drug company's academic partners, as well as indigent and/or uninsured patients. Thus, these sources of harm can be useful evidence in establishing that a preliminary injunction would be in the public interest.

⁴² Bloomberg News, "Wyeth Says It May Cut 10% of Jobs," *The New York Times*, January 26, 2008.

⁴³ Fishman-Lapin, "A diversifying Purdue Pharma hopes to regain control of its flagship drug," *The Stamford Advocate*, March 4, 2006.

⁴⁴ An Abbreviated New Drug Application is an application for a U.S. generic drug approval for an existing licensed medication or approved drug.

⁴⁵ *Pharmacia & Upjohn Co. v. Ranbaxy Pharm., Inc.*, 274 F. Supp. 2d 597 (n.D. Ill. 2003).

⁴⁶ *Pharmacia & Upjohn Co. v. Ranbaxy Pharm., Inc.*, 85 Fed. Appx. 205 (Fed. Cir. 2003).

⁴⁷ *Eisai Co. v. Teva Pharms USA, Inc.*, No. 05-05727 (D.N.J. 2008).

⁴⁸ *Eli Lilly & Co. v. Teva Pharms USA, Inc.*, 557 F.3d 1346 (Fed. Cir. 2009).

⁴⁹ *Sanifo-Synthelabo v. Apotex, Inc.*, 488 F. Supp. 2d 317 (S.D.N.Y.).

⁵⁰ *Sanifo-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368 (Fed. Cir. 2006).

⁵¹ *Purdue Pharma L.P. v. Boehringer Ingelheim GmbH*, 237 F.3d 1359 (2001 U.S. App).

⁵² *Abbott Laboratories v. Sandoz, Inc.*, 500 F. Supp.2d 807.

⁵³ *Abbott Laboratories v. Sandoz, Inc.*, 544 F.3d 1341 (Fed. Cir. 2008).

About the Author



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