Preliminary injunctions and compensation in pharmaceutical patent cases: the (blockbuster) UK damages claims for *Lyrica* (pregabalin)

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Introduction

Should a generic manufacturer be allowed to launch its product in the face of a patent asserted by pharmaceutical innovator, pending determination of that claim for patent infringement? That question is typically determined on an application for a preliminary or interim injunction (provisional measures), often brought urgently within hours or days of a launch or threatened launch.

What if such an injunction ends up being lifted at trial, for instance if the patent is found invalid or not infringed? Should the generic and/or third parties be compensated for the delay? That question is typically determined on a much more leisurely scale, years after the patent trial.

This article considers the relationship between these two key questions. It also looks at how the issue of compensation is due to be determined by the English Patent Court over the next few years in the complex set of damages claims in relation to Pfizer's Lyrica (pregabalin).

Should an interim injunction be granted?

There is an apparent degree of international agreement that the courts should have the power to issue an interim injunction to the patent owner in such cases.

Article 50 of the TRIPs Agreement requires courts to have the authority to order prompt and effective provisional measures to prevent infringement of intellectual property rights.[1] In the EU, that is mirrored in Article 9 of the IP Enforcement Directive 2004/48.[2]

However, the test applied by the courts on an application for provisional measures varies dramatically between jurisdictions. Even where the test is the same, its application can change over time and between jurisdictions.

In the United Kingdom, the courts use the test laid down by the House of Lords in *American Cyanamid* in 1975.[3] Similar tests are used in some other common law jurisdictions.

Under this test, the court first determines whether there is a serious question to be tried (in other words, that the claimant has a realistic, rather than fanciful, prospect of succeeding at trial). If so, the court does not try to determine the likely outcome at trial (no "mini-trial"). Instead, it tries to work out how to cause minimal harm if it gets the interim decision wrong. First, would damages payable by the defendant for infringement during the pre-trial period be adequate if the claimant succeeds at trial? If so, no interim injunction should be granted. If not, has the claimant undertaken to compensate the defendant and would damages under that "cross-undertaking" be adequate if the defendant succeeds at trial? If so, an interim injunction should be granted. If not, the court must proceed to determine the balance of convenience, considering all factors, including whether the defendant has

[1] WTO Agreement on Trade-related Aspects of Intellectual Property Rights 1994, 1867 UNTS 154.
[2] Directive 2004/48 [2004] OJ L157/32.
[3] *American Cyanamid v Ethicon* [1975] AC 396.

sought to "clear the way" by bringing proceedings to invalidate the patent and/or obtain a declaration of non-infringement.[4] If all the factors are evenly balanced, the court should favour the status quo.

In pharmaceutical patent cases, this has typically led to interim injunctions being granted in the United Kingdom, on the basis that there will normally be an irreversible price spiral if generics are permitted on the market.[5] However, that will depend on the evidence and it may not apply in exceptional cases.[6]

Applying a similar test, however, interim injunctions have recently been rejected in pharmaceutical patent cases in Australia[7] and Ireland,[8] although the Irish Supreme Court has since signalled a return to orthodoxy.[9]

Other jurisdictions can apply entirely different criteria when considering preliminary injunctions.

For instance, the Swedish Patent and Market Court rejected Mylan's request for a preliminary injunction for the melatonin patent, like the English Patents Court.[10] However, the Swedish court did not apply a balance of convenience test but instead rejected the application due to a lack of probable cause that patent was valid, following invalidation by the EPO Opposition Division (even though that decision was under appeal).[11]

In Germany, the Higher Regional Courts have typically required a high degree of confidence in both validity and infringement before granting a preliminary injunction. In the case of validity, they have generally required a positive first instance decision in EPO Opposition or national nullity proceedings. Whether that standard is compatible with Article 9 of the IP Enforcement Directive is the subject of a pending reference from the Munich Regional Court.[12]

Meanwhile, in the Netherlands, the District Court of The Hague recently granted a cross-border preliminary injunction, not only against the Dutch parent company and local subsidiary but against the French holder of the centralised marketing authorisation.[13] Such cross-border interim relief remains available under the recast Brussels Regulation on the recognition and enforcement of judgments.[14]

Then there are jurisdictions which have special frameworks for pharmaceutical patent litigation.

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[4] *SmithKline Beecham v Generics* [2001] EWHC 563 (Pat), pp11-12; *SmithKline Beecham v Apotex* [2003] EWCA Civ 137, [38]-[40]; *Novartis v Hospira* [2013] EWCA Civ 583, [60]-[64].

[5] *Warner-Lambert v Teva* [2011] EWHC 1691 (Pat); *MSD v Teva* [2012] EWHC 627 (Pat); in Scotland, *AstraZeneca v Teva* [2017] CSOH 150.

[6] See *Cephalon v Mylan* [2010] EWHC 2945 (Pat), refusing an interim injunction but ordering an expedited trial within 6 months; *Neurim v Mylan* [2020] EWCA Civ 793, refusing an interim injunction against Mylan's melatonin product on the "*extremely unusual facts*" of that case (para 54).

[7] *Sanofi-Aventis v Alpharma* [2019] FCAFC 28; *Mylan v Sun (No 2)* [2019] FCA 505.

[8] *Gilead v Mylan* [2017] IEHC 666; *Teva v Mylan* [2018] IEHC 324.

[9] *MSD v Clonmel* [2019] IESC 65.

[10] *Neurim v Mylan*, n.6 above

[11] *Neurim v Orifarm* (31 March 2020). See discussion by Serena Chang, Paul Abbott and Katherine Dudman "Spiralling into the abyss? Pharma PIs: lessons from Neurim" (https://riskandcompliance.freshfields.com/post/102gduu/spiralling-into-the-abyss-pharma-pis-lessons-from-neurim, last downloaded 12 April 2021).

[12] Case C-44/21 *Phoenix v Harting* (pending).

[13] *Novartis v Mylan* (29 September 2020).

[14] Regulation 1215/2012 [2012] OJ L351/1 (as amended), as determined by Case C-616/10 *Solvay v Honeywell* ECLI:EU:C:2012:445. The position is different for final relief where validity is in issue: Case C-4/03 *GAT v LuK* [2006] ECR-6509 and Case C-539/03 *Roche v Primus* [2006] ECR-6535.

The United States, of course, has linkage between the patent and regulatory systems and the Orange Book. Under the 1984 Hatch-Waxman Act, a patent owner will typically benefit from an automatic 30 month stay during the patent litigation.[15] Preliminary injunction issues only arise after that 30 month period, and typically the status quo will be preserved by consent in such cases if trial is near.[16]

Canada has a similar linkage regime, although the stay in Canada is only 24 months.[17]

Should compensation be awarded?

Again, there is a degree of international agreement on the broad principle, but great variation in the detail.

Article 50(7) of TRIPs provides that "*Where the provisional measures are revoked or where they lapse due to any act or omission by the applicant, or where it is subsequently found that there has been no infringement or threat of infringement of an intellectual property right, the judicial authorities shall have the authority to order the applicant, upon request of the defendant, to provide the defendant appropriate compensation for any injury caused by these measures.*"

That language is mirrored in Article 9(7) of the IP Enforcement Directive 2004/48.

There have been relatively few UK judgments on damages under cross-undertakings, and frequently these have been procedural rather than final judgments.[18] Pure monetary claims, much like claims for damages for patent infringement, are typically settled before trial, not least because of the "loser pays" principle in relation to the costs of such proceedings. That may now change, as discussed further below.

In Canada, there is statutory provision for damages to be paid for losses caused during the automatic stay,[19] which has been analogised to the cross-undertaking approach.[20] Interesting issues arose in relation to ramipril, where both Apotex and Teva claimed damages under that provision for having been kept off the market.[21] The trial judge found that she did not have to apply a single "but for" world, but constructed different hypothetical worlds for each claim, and this was upheld by the Court of Appeal and Supreme Court against the patentee's challenge. These cases have been followed in cases relating to olanzapine and pregabalin.[22]

In Australia, a detailed cross-undertaking damages claim was determined in 2018 in *Sigma v Wyeth*.[23] Notably, the judge remarked in the penultimate paragraph of her 296-page judgment (plus schedules) as follows:[24]

> "*It is difficult to imagine that when Sundberg J and then I granted the interlocutory injunctions in 2009 we anticipated that if those injunctions turned out to be wrongly granted, the resulting exercise would bear any resemblance to this one. Hindsight makes one thing certain. Knowing*

[15] 21 USC §355(j)(5)(B)(iii).
[16] See David Blackburn and Rasmus Jørgensen "Economics in Life Sciences: Does Temporary Generic Competition Have a Lasting Impact on Branded Drug Sales?" (NERA, 18 March 2021) for an interesting economic discussion of the issues with such preliminary injunctions in the US market.
[17] Patented Medicines (Notice of Compliance) Regulations, regulation 7(1)(d).
[18] *SKB v Apotex* [2006] EWCA Civ 658; *Servier v Apotex* [2014] UKSC 55; *AstraZeneca v KRKA* [2014] EWHC 84 (Pat); *Napp v Dr Reddy's* [2017] EWHC 1433 (Pat) and [2019] EWHC 1009 (Pat).
[19] Patented Medicines (Notice of Compliance) Regulations, regulation 8(2).
[20] *Apotex v Merck* 2008 FC 1185, [54]; *Apotex v Astrazeneca* 2012 FC 559, [58].
[21] *Teva v Sanofi-Aventis* 2014 FCA 67; *Apotex v Sanofi-Aventis* 2014 FCA 68 and 2015 SCC 20.
[22] *Eli Lilly v Teva* 2018 FCA 53; *Pfizer v Pharmascience* 2020 FCA 55.
[23] *Sigma v Wyeth* [2018] FCA 1556.
[24] Ibid., [1336].

> *what has occurred, it could never have been concluded, for example, that insofar as relevant to the balance of convenience it would be easier for the generics to prove their loss if the interlocutory injunctions were wrongly granted than for Wyeth to prove its loss if the interlocutory injunctions were withheld and the method patent was valid.*"

That judgment has been relied on by the Australian courts when refusing preliminary injunctions in later cases.[25] The Australian Government has also run into difficulties when seeking to claim under cross-undertakings.[26]

However, there appears to be a significant common law/civil law divide when it comes to damages in such cases. While damages are typically available across mainland Europe, in line with the IP Enforcement Directive, they are likely to be awarded at a much lower level.

Indeed, the circumstances in which any damages are available may now be limited, following the consideration of Article 9(7) of the IP Enforcement Directive in the *Bayer* judgment of the CJEU.[27] The Court ruled there that compensation need only be paid if the applicant has "abused" the provisional measures and procedures, taking due account of all of the objective circumstances of the case, including the conduct of the parties. It is necessary but not sufficient that the provisional measures have been repealed, for instance because the patent was found invalid. To require otherwise could discourage the use of provisional measures and would "*run counter to the Directive's objective of ensuring a high level of protection of intellectual property*".

This is more in line with the approach in the US, where damages may arise under antitrust but only in exceptional cases. However, if the first generic filer is successful it will receive 180-day co-exclusivity with the patent owner.[28]

In the light of that judgment, the approach to the availability of damages may need to be revisited in countries bound by the IP Enforcement Directive, including in particular Ireland and (pending any domestic change to the law) the UK.

The UK *Lyrica* (blockbuster) damages claims

In the meantime, the issue of appropriate compensation is now before the English Patents Court in mammoth proceedings relating to Lyrica (pregabalin).

Product and patents

The case is well known to patent lawyers. Pfizer obtained a marketing authorisation for Lyrica (pregabalin) in July 2004. In Europe, Lyrica was initially indicated for the treatment of peripheral neuropathic pain and epilepsy, and the indication was extended to generalised anxiety disorder in March 2006 and to central neuropathic pain in September 2006. Lyrica became a blockbuster drug: in 2013 its global sales were around $4.6bn, of which its UK sales were around $312m.[29]

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[25] *Sanofi-Aventis v Alpharma* and *Mylan v Sun (No 2)*, n.7 above. See Rebekah Gay et al "Where is the balance now? Preliminary injunctions in pharmaceutical patent proceedings in 2020 and beyond" (https://hsfnotes.com/ip/2020/07/15/where-is-the-balance-now-preliminary-injunctions-in-pharmaceutical-patent-proceedings-in-2020-and-beyond/, last downloaded 12 April 2021).

[26] *Commonwealth of Australia v Sanofi (No 5)* [2020] FCA 543.

[27] Case C-688/17 *Bayer v Richter Gideon* EU:C:2019:722, discussed by Felthun et al in (2020) 17(6) BSLR 234-239.

[28] 21 USC §355(j)(5)(B)(iv).

[29] NHS England Points of Claim, para 12.

For present purposes, Pfizer had three key layers of protection in the UK: data exclusivity, a compound patent and a second medical use patent.

First, under the rules on data exclusivity which then applied, applications for generic pregabalin could not be filed until 10 years after the first authorisation. That meant no generic applications could be filed before July 2014.

Second, Pfizer had a compound patent which covered pregabalin itself.[30] That patent expired in May 2013. A supplementary protection certificate (SPC) had been granted, which would not expire until May 2018. However, Pfizer did not pay the fees for the SPC and so it too lapsed in May 2013.

Third, Pfizer had another patent, EP(UK) 0,934,061, which covered the use of pregabalin for the preparation of a pharmaceutical composition for treating pain (claim 1) and neuropathic pain (claim 3), among others (a Swiss-form second medical use patent). That patent would expire in July 2017 and was not covered by an SPC.

Generic challenge and launch in 2014-2015

The lapse of the SPC opened a window for generic entry from 2015 to July 2017 for those who were willing to take on the second medical use patent. It also opened the market up fully from August 2017.

Mylan brought proceedings to revoke EP '061 on 24 June 2014 and Actavis followed on 12 September 2014.

The first generic companies then launched with "skinny labels", only indicating use for epilepsy and generalised anxiety disorder, but not for pain. Nevertheless, they were sued for infringement of the patent based on the claims to pain and neuropathic pain. On 8 December 2014, Pfizer sued Actavis for threatened infringement by launch of a skinny label, but an interim injunction was refused on 21 January 2015.[31] Pfizer also sued Teva on 9 February 2015. Following that, there were launches by Dr Reddy's on 13 February 2015 (leading to suit by Pfizer on 17 February 2015) and Actavis on 17 February 2015.

Pfizer's concern was that doctors in the UK normally prescribe by the generic name, without reference to the indication, and that pharmacies would therefore fill those prescriptions with generic products even if the prescription was for pain, notwithstanding any skinny label. Given the refusal of interim injunctions against the skinny label manufacturers, Pfizer also took action to prevent the National Health Service from prescribing and dispensing generic pregabalin for pain. This included correspondence from September 2014 and ultimately a decision on 26 February 2015 (with reasons following on 2 March 2015) requiring the NHS in England to issue guidance that prescriptions of pregabalin for neuropathic pain should be by the brand name Lyrica rather than the generic name pregabalin.[32] Similar guidance followed in Wales and Northern Ireland in March 2015. No such guidance followed in Scotland.

Some months later, Sandoz launched on 26 June 2015 followed by Teva on 3 July 2015.

[30] That patent also claimed the use of pregabalin in the manufacture of anti-convulsant, anti-anxiety and anti-psychotic medicaments (Swiss-form first medical use claims).
[31] *Warner-Lambert v Actavis* [2015] EWHC 72 (Pat), upheld in *Warner-Lambert v Actavis* [2015] EWCA Civ 556.
[32] *Warner-Lambert v Actavis* [2015] EWHC 485 (Pat).

The patent was then partially revoked by the Patents Court on 10 September 2015,[33] and Pfizer's application to limit claim 3 to peripheral neuropathic pain was rejected on 25 November 2015.[34] However, Pfizer managed to uphold the validity of claims 10-12 (trigeminal neuralgia, acute herpetic and postherpetic pain and causalgia pain respectively) as specific types of peripheral neuropathic pain.

Following the first instance judgment, in October 2015 Sandoz launched under a full label, this time including the pain indications. That was immediately the subject of an interim injunction application by Pfizer, against both Sandoz and the Lloyds pharmacy chain, which was granted on 4 November 2015.[35]

Meanwhile, Mylan had launched its own skinny label on 16 October 2015.

Finally, Ranbaxy had also been planning to launch under a full label but, following the decision against Sandoz, agreed with Pfizer on 4 December 2015 not to do so, upon provision of a cross-undertaking by Pfizer.

Appeals 2016-2018

The first instance judgment was appealed but ultimately upheld by the Court of Appeal in October 2016.[36]

Following the Court of Appeal judgment, Sandoz sought to vary the terms of the interim injunction preventing sale under its full label, but this was rejected.[37]

The Supreme Court then also upheld the judgment in November 2018,[38] save that it extended the scope of revocation by finding that the patent application did not make it plausible that pregabalin would work with peripheral neuropathic pain, rendering claims 10-12 also invalid.[39]

Damages claims

The process was started by Dr Reddy's, which applied for directions in January 2020. This led to all beneficiaries of cross-undertakings being invited to attend a first Case Management Conference in July 2020, and the parties exchanging detailed points of claim, points of defence and points of reply before being invited to a further Case Management Conference in December 2020.

As a result, the National Health Service bodies and five of these six generic groups are now seeking damages.[40] The claims by the generic groups (other than Ranbaxy) raise liability not only under the cross-undertakings but also as a result of the communications by Pfizer to health authorities and pharmacists between October 2014 and February 2015.[41] The potential liability for such

[33] *Mylan v Warner-Lambert* [2015] EWHC 2548 (Pat).
[34] *Mylan v Warner-Lambert* [2015] EWHC 3370 (Pat). Both these decisions were ultimately upheld and extended by the Court of Appeal and the Supreme Court, as discussed further below.
[35] *Warner-Lambert v Sandoz* [2015] EWHC 3153 (Pat).
[36] *Warner-Lambert v Mylan* [2016] EWCA Civ 1006.
[37] *Warner-Lambert v Sandoz* [2016] EWHC 3317.
[38] *Warner-Lambert v Mylan* [2018] UKSC 56.
[39] Ibid., [47]-[54].
[40] Mylan is not – it is not clear whether they have settled with Pfizer, as Lloyds have done.
[41] *Mylan v Warner-Lambert* [2015] EWHC 2548 (Pat), [690]-[721], which considered whether the communications would have been regarded as threats of proceedings for patent infringement which aggrieved Actavis. This aspect of the first instance judgment was not appealed.

communications at that time arose under section 70(1) of the Patents Act 1977, which read as follows:[42]

> *Where a person (whether or not the proprietor of, or entitled to any right in, a patent) by circulars, advertisements or otherwise threatens another person with proceedings for any infringement of a patent, a person aggrieved by the threats (whether or not he is the person to whom the threats are made) may, subject to subsection (4) below, bring proceedings in the court against the person making the threats, claiming any relief mentioned in subsection (3) below.*

The sums claimed by the five generic groups are very significant, with the total approaching £1bn.

Claimant[43]	**Sum claimed**[44]
NHS England	£628 million
NHS Wales	£43 million
NHS Northern Ireland	£45 million
NHS Scotland	(not provided)
Dr Reddy's	£35 million
Actavis	£29 million
Sandoz	£11 million
Teva	£6 million
Ranbaxy	(confidential)
Mylan	*Not pursuing*
Lloyds	*Settled*[45]
TOTAL (where disclosed)	**£797 million**

Following the December 2020 hearing, a three-trial process has now been set down to determine these claims.[46] First, in June 2021, a four-day trial will take place to consider the possible counterfactual assumptions as preliminary issues. Second, in June/July 2022, a 25-day trial will take place to decide common issues between the claims. Finally, in April/May 2024, a 20-day trial will take place to determine all remaining issues, including those of quantum.

Even reading these directions makes clear the complexity of these proceedings. For instance, the possible counterfactual assumptions include: (a) which of the threats, orders and undertakings should be deemed made in each counterfactual; (b) whether it should be deemed known that the relevant claims of the patent were invalid and (c) at what point full label launches would have been permitted. Subject to the outcome of those preliminary issues, the common issues trial would then focus more on the prices which would have been paid and the distribution of volume between Lyrica and the various generic manufacturers (including those not participating in the claims).

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[42] The unjustified threats provisions were amended by the Intellectual Property (Unjustified Threats) Act 2017. However, it remains the case under s70C(1)(c) as amended that "*Proceedings in respect of an actionable threat may be brought against the person who made the threat for… damages in respect of any loss sustained by the aggrieved person by reason of the threat.*"

[43] Several of the Points of Claim are unavailable on the court's ce file website. The majority have been kindly provided by the parties' representatives, although those from NHS Scotland had not yet been provided at the time of writing.

[44] Rounded to nearest million.

[45] *Warner-Lambert v Sandoz* [2016] EWHC 3317, [21].

[46] Directions Order of 18 December 2020, sealed on 25 January 2021.

Conclusion

The court and parties involved in the *Lyrica* damages claims are clearly seeking to learn lessons from previous determinations of similar damages elsewhere, in particular in Australia and Canada. There may also be useful lessons in the field of antitrust damages claims, where there are complex issues of direct and indirect purchasers, pass-on and multiple counterfactuals. Determining the claims together may help avoid inconsistent results, which have arisen in Canada, but it does not make the process quick nor easy. Damages arising between 2015 and 2017 are not going to be determined at first instance until at least 2024. In the UK, the NHS will have to determine whether this is an attractive route for future litigation to recover resources, as it is doing in its long-running antitrust damages litigation.[47]

This article has looked separately at issues of interim injunction and damages. However, they are clearly related, as has been most evident in the Australian courts. It is important at a policy level that the system functions as a cohesive whole, while taking into account the policy issues relied upon by the CJEU in *Bayer* to limit the scope for damages to cases of abuse.

Cohesion is also important at a practical level. As might be expected, some of the claimants have relied heavily on the evidence put in by Pfizer's lawyers when seeking interim injunctions about the likely scale of generic entry. Indeed, the overall size and relative distribution of the sums claimed support the view that generic entry is likely to lead to an irreversible price spiral, primarily to the benefit of the healthcare payor. Nevertheless, parties involved in preliminary injunction disputes need to keep in mind the longer term as well as the short term.

More broadly, when considering potential cross-border patent litigation in pharmaceutical cases and beyond, initial strategy discussions have for many years focussed on the prospects of preliminary injunctions and the potential consequences if these are later overturned, and how that varies between countries. The changing landscape, both in common law and civil law jurisdictions, mean those questions still need to be asked, as the answers are continually changing. Equally, when answering those questions, it is important to be aware of developments elsewhere, given that these may be considered and even adopted by domestic courts and judges.

[47] See most recently *Secretary of State for Health v Servier* [2020] UKSC 44, an appeal to the Supreme Court on preliminary issues in claims filed in 2011-2012 concerning patent settlements entered into between 2005 and 2007.