Second medical use claims and 'skinny' labels: clear guidance at last?

“...UK courts ... consider whether a patent claim to an approved second medical use of a pharmaceutical can be infringed where a competitor’s product is marketed with a so-called ‘skinny’ label...”

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The ongoing litigation between Pfizer and a number of generic companies over the last 18 months has provided UK courts with the first proper opportunity to consider whether a patent claim to an approved second medical use of a pharmaceutical can be infringed where a competitor's product is marketed with a so-called 'skinny' label that mentions off-patent uses only. While the appeal of the First Instance Patents Court's substantive decision is yet to be heard, the decisions so far have provided valuable guidance as to how the courts may interpret such claims [1]. They also suggest the steps generic companies may have to take to avoid infringement.

Pregabalin

Pregabalin is the active ingredient of the Warner Lambert (now Pfizer) product Lyrica®, which was approved in the EU for three medical indications: treatment of epilepsy, generalized anxiety disorder (GAD) and neuropathic pain. The first two indications were disclosed and encompassed by the claims of the basic patent covering the compound itself, which expired in 2013. Neuropathic pain was an indication covered by the claims of a second medical patent [2] extending beyond the expiry dates of both the basic patent, and EU data exclusivity.

'Swiss-form' claims

The use claims of the neuropathic pain patent were in the 'Swiss-type' format:

'Use of (pregabalin) in the manufacture of a medicament for treating (neuropathic) pain'.

Swiss-type claims were first allowed by the European Patent Office (EPO)'s Enlarged Board of Appeal in its landmark first case [3]. Although medical use claims in this format are not permitted by the EPO in patent applications filed from 2011 onward, Swiss claims will be still with us for some time and cover second medical uses of a large number of marketed pharmaceuticals.

'Skinny' labels

European pharmaceutical regulatory law [4] allows generic pharmaceutical companies who have received abridged marketing authorizations to omit from their labels any medical indications that are the subject of second medical use patents – such a label is commonly known as a ‘skinny’ label. However, before the pregabalin litigation it was far from clear whether a skinny label would enable generics to avoid infringement of second medical use patents in the UK, nor whether they would need to take further steps to avoid infringement.

Infringement of patents in the UK

It was not disputed in the litigation that Swiss-type claims relate to a process of manufacture, rather than to a product of that process as such. However, in Europe, a process patent is directly infringed by the marketing of a product produced directly

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by that process, regardless of where the product is made [5].

Patents of all types are also indirectly infringed by the supply or offer to supply of a means relating to an essential element of the invention, where that means is suitable and intended for putting the invention into effect. Importantly, for indirect infringement in the UK, both the supply and intended use must be in the UK [5].

The interim skirmishes

Following expiry of the basic patent and data exclusivity periods, a number of generics companies, led by Actavis, announced their intention to market pregabalin with a 'skinny' label omitting the neuropathic pain indication. They also indicated they would seek revocation of the second medical use patent before marketing the drug with a full label for all approved indications. Pfizer in turn sought interim injunctions, under the second medical use patent, aimed at preventing generic entry into the market. Both sides took steps to inform health authorities and pharmacists of their intentions prior to trial, in particular to indicate that the generic drug should not be prescribed for treating pain.

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In the interim decisions, the judges in the First Instance Patents Court [6,7] and in the Court of Appeal [8] expressed different views on how second medical use claims in Swiss form should be interpreted, and on indirect infringement of such claims.

In the Patents Court, the judge allowed the direct infringement claim, which arose from the sale in the UK of the direct product of the process of manufacture noted above, to continue to full trial. However, he indicated it would be likely to fail on the basis that, as he interpreted such claims, 'for the treatment of Y' requires a subjective intention on the part of the generic manufacturer that its product will be used for that treatment. Pfizer's claim of indirect infringement on the other hand was initially struck out. This was on the basis that because the Swiss-form claims were to a process of manufacture, and the claimed process (the invention) was not being put into effect in the UK since the drug was being made outside the UK, there could be no indirect infringement through the supply in the UK of 'means relating to an essential element' of that process invention [6].

On appeal from that interim decision, the Court of Appeal indicated that in its view as regards to direct

infringement, 'for' meant either subjective intent or, if that subjective intent was not present, that the ultimate intentional use of the drug for the patented indication was reasonably foreseeable by the manufacturer [8]. It was suggested that off-label prescribing and/or dispensing of generic pregabalin for neuropathic pain was reasonably foreseeable, regardless of the generic company's specific intention and skinny label. The Court of Appeal also reinstated the indirect infringement claim, although it did express some doubts as to its merits.

Full trial judgment at First Instance: direct & indirect infringement of Swiss-form claims

In the full trial before the Patents Court [9], the judge (Mr Justice Arnold) found the relevant claims invalid on the ground of insufficiency, meaning that unless this aspect of the case is overturned on appeal, the infringement discussion is somewhat academic. However, the judge considered the various potential interpretations of Swiss-form claims in some detail.

The Patents Court considered both its own and the Court of Appeal's interpretations from the interim proceedings. Regarding his own interpretation that there must be a subjective intention for direct infringement, the judge found that it was clear that Actavis never had that intention, given all the steps they had taken to try to prevent or at least mitigate unauthorized use.

As regards to the Court of Appeal's interpretation and approach, the judge had to consider the position concerning reasonable foreseeability (by Actavis) of an ultimate intentional off-label use (by doctors or pharmacists) at various times in the history of Actavis' development and launch of its product. Also relevant was the history of the dispute between the parties, bearing in mind how Actavis' state of knowledge and actions altered over that time. Having done so, aside from a negligibly small number of circumstances where such use was foreseeable very early on, he concluded, on the facts, that at no stage was such intentional use foreseeable by Actavis, bearing in mind the specific steps taken by Actavis, over and above the skinny label, since the issue first arose.

Accordingly, the judge held that Actavis was not liable for direct infringement on either interpretation. Relevant to these conclusions were that Actavis had both used a skinny label for its product and taken steps to notify superintendent pharmacists that its drug was not licensed for the patented indication.

As regards to indirect infringement, having addressed all of the Court of Appeal's reasoning, Mr Justice Arnold confirmed his original decision that there was no indirect infringement by Actavis because the 'invention' was a process of manufacture, and that

process was not being put into effect in the UK by anyone, nor was there any prospect that it would be.

Prescribing changes: a clear way out?

Second medical use patents are generally accepted, at least in Europe (although not worldwide), as a necessity to reward continued investment and research and innovation into known pharmaceuticals. However, the extent to which they can be enforced brings policy, as well as legal, issues. There clearly must be a way in which innovators can enforce second medical use patents against competitors, otherwise they are effectively worthless. However, generic companies have the lawful right to market the drug for off-patent uses – allowing second medical use patents to restrain such lawful activity could effectively amount to repatenting the drug itself by the back door.

At the end of Mr Justice Arnold’s judgment, he expressed a note of what appears to be exasperation at the need for a system to address these conflicting policy issues surrounding second medical use inventions. He sees the solution less in extended patent litigation than in altering the prescribing practice for second medical indications.

His suggestion was that the drug be prescribed by its generic name for off-patent uses, but by brand name for patented (second) medical uses.

However, at least in the UK, prescribing is not within the manufacturer’s control – this requires centralized guidance from health authorities. The NHS intervened in these proceedings and noted the desirability of this approach as a sensible solution.

The Court of Appeal is set to hear the appeal of the full trial judgment in May 2016. Given the various legal issues involved and the fundamental public importance of the case, it is likely the case will eventually be heard by the UK Supreme Court. However, the common sense solution proposed by the Patents Court may give both innovators and generics some guidance on the way through this complex maze.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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- 4 Directive 2001/83/EC (2001).
- 5 *Patents Act 1977*, sections 60(1)(b) and (c) and 60(2) (1977).
- 6 *Warner-Lambert v. Actavis & others*: EWHC 72 (2015).
- 7 *Warner-Lambert v. Actavis & others*: EWHC 485 (2015).
- 8 *Warner-Lambert v. Actavis & others*: EWCA Civ 556 (2015).
- 9 *Warner-Lambert v. Actavis & others*: EWHC 2548 (2015).