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PI maintained against Sandoz' full-label pregabalin product

Brian Cordery (Bristows) · Thursday, December 22nd, 2016

by Steven Willis

Yesterday, the Patents Court handed down yet another decision in the Sisyphean pregablin litigation, this time refusing Sandoz' application to vary the Order for Injunction which resulted from Arnold J's October 2015 decision ("*Sandoz I*") to injunct Sandoz following its launch of a full label pregabalin product ("Pregabalin Sandoz"). As is typically the case when writing about pregabalin, it is necessary to recount a chunk of procedural history and inter-party correspondence before I get to the crux of the decision at hand so please bear with me (or skip ahead to paragraph 7).

Prior to *Sandoz I*, Arnold J had held a number of claims of Warner-Lambert's patent for the use of pregabalin in pain invalid including claim 1 (pain) and claim 3 (neuropathic pain) ("*Warner-Lambert V*" according to Arnold J's nomenclature). A number of subsidiary claims to various types of pain, including several types of neuropathic pain (claims 10-12) were held to be valid. Of the valid subsidiary claims, only those which are a subset of neuropathic pain cover indications which are included in the marketing authorisation for Warner-Lambert's pregabalin product ("Lyrica").

Subsequent to *Sandoz I*, the Court of Appeal upheld Arnold J's judgment on validity in all material respects ("*Warner-Lambert CA II*"). The Court of Appeal took a different approach to Arnold J on infringement and indicated that it would have reached a different conclusion (i.e. that the patent would have been infringed had it been valid). However, in light of the validity findings (Warner-Lambert seemingly only asserted claims 1 and 3), these comments were only obiter. The Court of Appeal refused permission to appeal to the Supreme Court but Warner-Lambert has applied directly. It was common ground before Arnold J that the Supreme Court is unlikely to make a decision on this application before mid-January 2017 at the earliest. In the event that permission is granted, Actavis and Mylan have applied for permission to cross-appeal the findings on validity in relation to claims 10-12.

In February 2015, Arnold J had ordered the NHS to issue guidance on prescription practices with a view to ensuring that skinny label pregabalin products were not dispensed "cross-label" in the treatment of the patented indications. Following *Warner-Lambert CA II*, Warner-Lambert sought to engage the NHS with a view to revising this guidance. Warner-Lambert requested that the NHS direct that pregabalin should be prescribed by brand name (thereby ensuring that Lyrica be dispensed) for any of the indications covered by a claim which had been held valid (i.e. not just those for which Lyrica is approved).

The NHS initially agreed to amend its guidance accordingly. However, a number of generic pharmaceutical companies took issue with the proposed guidance and suggested that it may amount to a breach of the ABPI Code or Directive 2001/83 as it amounted to a promotion of Lyrica for off-label purposes. The NHS subsequently indicated a need to consider the issues further at a "senior clinical level". Nothing more was heard from the NHS as of the date of the hearing, which Arnold J regarded as "unfortunate".

In addition to seeking to revise the NHS Guidance, Warner-Lambert made a concession to allow generic companies to obtain "intermediate marketing authorisations" whereby they were entitled to extend their authorised indications to include central neuropathic pain (held not to be plausibly disclosed in *Warner-Lambert V* and *Warner-Lambert CA II*) but not peripheral neuropathic pain (held to be plausibly disclosed, but without any benefit to the validity of claim 3).

Against this backdrop, Sandoz sought to vary the terms of the Order arising out of Sandoz I, such that it would be entitled to launch Pregabalin Sandoz subject to the proviso that it would not offer for sale, sell or supply the product for conditions for which Lyrica is authorised and for which Warner-Lambert maintains valid claims following the Court of Appeal decision (i.e. acute herpetic and postherpetic pain or causalgia pain). Sandoz further offered to take certain steps to minimise the chances that its product would be so used.

A threshold condition for Sandoz to succeed in its application was the requirement to show that there had been a "material change" in circumstances since Sandoz I. Arnold J did not consider that the Court of Appeal's decision to uphold his decision to revoke claims 1, 3, 4, 6, 13 and 14 of the patent in Warner-Lambert CA II was material. He did however consider that Warner-Lambert having stated that it would not prevent Gx from marketing pregabalin for indications which are only protected by claims which were held invalid by the Court of Appeal did amount to a material change as it enabled Sandoz to advance its case on proportionality. The Court further considered that there were two other factors that it needed to take into account, notwithstanding that they had not been raised by Sandoz: (i) Warner-Lambert's infringement action against Sandoz has been stayed and the March 2016 trial date has been vacated; and (ii) the Court of Appeal has given further consideration to the law relating to infringement of Swiss-type claims.

Having held that there had been a material change since Sandoz I, Arnold J revisited the assessment as to Warner-Lambert's entitlement to an interim injunction. Sandoz focussed on "proportionality" and in particular the importance of the Court including consideration of "whether the injunction was proportionate and a legitimate barrier to trade", citing **Napp v Dr Reddy's** [2016] EWHC 1517 (Pat) and C-494/15 **Tommy Hilfiger**. In relation to the latter, Arnold J accepted Sandoz' submission that Article 3(2) of Directive 2004/48/EC ("the Enforcement Directive"), which concerns the need for enforcement measures to be proportionate, was directed not only to Member States' legislatures but also to national courts when considering whether or not to grant an injunction.

Arnold J then went on to hold that there was a serious issue to be tried in relation to Claims 10 ("trigeminal neuralgia"), 11 ("acute herpetic and postherpectic pain") and 12 ("causalgia pain"). All three are types of peripheral neuropathic pain. Pregabalin Sandoz is indicated for peripheral neuropathic pain. Furthermore, it refers to post-neuropathic neuralgia at paragraph 5.1 of its SmPC.

In the assessment of irreparable harm, Sandoz relied upon the fact that the indications covered by claims 10, 11 and 12 amounted to only 1.13% (or £2.3 million between now and the expiry of the

patent in July 2017). Arnold J held that even though the claims covered only a small percentage of the market, if the marketing of pregabalin Sandoz infringes the claims, Warner-Lambert is prima facie entitled to an injunction. Furthermore, Arnold J accepted that if Sandoz was allowed to launch, other Gx would launch full label products which would result in a "*free-for-all in the full label market*". Arnold J did not consider that the "further steps" offered by Sandoz to preclude Pregabalin Sandoz being used in the treatment of the conditions covered by claims 10, 11 and 12 "*materially affected the harm which Warner-Lambert will suffer*". As such, he maintained his position that the risk of irreparable harm to Warner-Lambert was greater than to Sandoz.

Turning to the balance of convenience, Arnold J accepted Warner-Lambert's submission that Sandoz' failure to clear the way and the preservation of the status quo were factors which favoured the grant of the injunction and that this remained the case. Furthermore, Arnold J considered that Sandoz' arguments on proportionality (i.e. that claims 10, 11 and 12 covered only a small percentage of the market) ignored the fact that claims 2, 5, 7, 8 and 9 were also upheld and that these claims amount to 13.8% of the market. The fact that Lyrica is not authorised for these conditions was "*immaterial*". Arnold J also referred to the fact that Sandoz has the benefit of Warner-Lambert's cross-undertaking.

Arnold J ultimately refused Sandoz' application for the PI to be lifted; maintaining the injunction was more likely to cause the least irremediable prejudice. However, he noted that an assessment of Warner-Lambert's entitlement to a final injunction may have reached a different conclusion.

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