News and Views

A landmark case for second medical use patents in the UK

Summary

On 28 May 2015, the UK Court of Appeal issued its judgement in an appeal by Warner-Lambert against a decision of the UK High Court that refused to grant a preliminary injunction aimed at preventing sales of a "skinny label" pregabalin product for which Actavis had sought a Marketing Authorisation.

Although largely positive, the decision of the UK Court of Appeal represents mixed news for innovators.

The good news relates to the standard for proving infringement that was adopted by the Court of Appeal, which now compares very favourably to the much stricter standard for proving anticipation of second medical use claims (which has since been confirmed by a decision of the UK High Court in a different case).

On the other hand, the less positive news relates to:
- the difficulties that are likely to be encountered in seeking preliminary injunctions against "skinny label" generic products; and
- the possibility that, even for innovative medicinal products that are marketed in the UK, freedom-to-operate issues may arise in respect of patents to indications that are not on the product label.

These issues (and others, including crucial questions that have not yet been answered) are discussed in more detail below.

Background: the dispute

The background to the dispute between Warner-Lambert and Actavis, as well as the decision of the UK High Court that was the subject of the above-mentioned appeal, is described in an article written by Mike Snodin entitled "*When public policies collide: the battle to enforce second medical use patents for drugs in Europe*", which was first published in *Scrip Regulatory Affairs* on 24 March 2015. A copy of the article can be viewed here.

In short, Actavis applied for a marketing authorisation for Lecaent®, a pregabalin product that omitted from its label one of the indications (neuropathic pain) found on the label of the reference product (Lyrica®).

Whilst the label for Lecaent® did not mention neuropathic pain, prescribing and dispensing practices for medicines in the UK meant that it was likely (or at least that it could not be ruled out) that Lecaent® would be used for the treatment of neuropathic pain. Warner-Lambert therefore alleged that sale of Lecaent® would infringe an in-force patent (EP 0 934 061 B3) containing "Swiss" format second medical use claims that encompass the use of pregabalin for the preparation of a pharmaceutical composition for treating (neuropathic) pain.

Highlights of the decision

- Warner-Lambert argued that they would suffer irreparable harm if the court did not grant a preliminary injunction preventing the sale of Lecaent®. Nevertheless, the Court of Appeal confirmed that the lower court was correct to not grant such an injunction.

- A key point weighing against the issuance of an injunction appears to have been Warner-Lambert's likely (and then actual) success in persuading the lower court to compel NHS England to issue guidance that, for the treatment of neuropathic pain, pregabalin should only be prescribed by reference to the brand name Lyrica®.

- Whilst agreeing that "Swiss" format claims relate to a process and are directed at a manufacturer, the Court of Appeal overturned the lower court's finding that a subjective intent on the part of the manufacturer is required in order to infringe such claims.

- The Court of Appeal instead decided that "Swiss" format second medical use claims can be infringed if it is **reasonably foreseeable** that the generic product would be dispensed for the patented indication.

Further development

On 24 June 215, the UK High Court issued a decision in *Hospira v Genentech* ([2015] EWHC 1796 (Pat)). Amongst other things, that decision addresses the standard for assessing novelty of claims in second medical use format, and is the first case to do so in the UK since the Court of Appeal decision in the *Warner-Lambert v Actavis* case.

Significantly, the UK High Court assessed the novelty of the "Swiss" format second medical use claims according to the principles of the "settled" case law of the European Patent Office. Under that case law, a prior art disclosure only anticipates a claim in second medical use format if it indicates that the claimed therapeutic effect is actually achieved. An example of the logic behind this conclusion is provided in paragraph 98 of the decision in *Hospira v Genentech*, which states that:

"*...one cannot intend to administer the combination of trastuzumab and a taxane to achieve increased efficacy in the treatment of breast cancer compared to the taxane alone* ***unless one knows that that clinical benefit will be obtained***" (emphasis added).

Thus, whilst the appeal decision in the *Warner-Lambert* case has set a new standard in the UK for assessing infringement of second medical use claims, the standard for assessing novelty of those claims remains unchanged.

Commentary

Enforcement of second medical use patents

It should now be much easier for the holders of second medical use patents to enforce their rights in the UK (including against "skinny label" generic products).

However, crucial questions remain, such as:
(1) when (if ever) a preliminary injunction will be granted in respect of a "skinny label" generic product;
(2) how (if at all) a manufacturer of a generic product can avoid infringing a patent to an indication omitted from the "skinny" label for that product; and
(3) whether the patentee will be awarded damages, an account of profits or a reasonable royalty in respect of sales of a "skinny label" generic product found to infringe his patent.

Question 3 is particularly important, as how it is answered may well dictate:
- the extent to which a patent to a second medical use can be used to defend an income stream in respect of the patented indication; and
- the circumstances under which it will be economically viable for a generic manufacturer to market a "skinny label" product.

It should not be long before preliminary answers to Question 3 are provided, as that question is likely to be considered during the full trial on pregabalin that starts with a hearing at the UK High Court at the end of June 2015.

It may take significantly longer for final answers to Questions 1 and 2 to emerge, as the first instance decision in the full trial is almost certain to be appealed – perhaps even up to the level of the Supreme Court in the UK.

With regard to Question 1, however, it is important to note that the relief granted to Warner-Lambert (against NHS England, requiring them to issue prescribing guidance) ought to be available to others in similar circumstances. The availability of that relief was one of the key reasons for the courts refusing to grant a preliminary injunction. It is therefore perhaps unlikely that such injunctions will be issued in respect of other "skinny label" generic products in the near future.

Disharmony across Europe

It is likely to take a number of years before there is any degree of harmonisation across Europe on this important area of law. This is because:

- the decision of the UK Court of Appeal points to ***direct*** infringement of a second medical use claim by a "skinny label" generic product; whereas
- recent court rulings in Germany and the Netherlands point to ***indirect*** infringement under similar circumstances.

It will be important for the current disharmony to be resolved, as this could otherwise create difficulties for the Unified Patent Court (if and when that Court comes into existence).

The value of patents to second medical uses

Above all, the appeal decision in the *Warner-Lambert* case in the UK has confirmed the importance and value of second medical use protection in Europe, particularly in view of:
- the ease of proving infringement (to a reasonably foreseeable standard);
- the relative difficulty of proving anticipation (to a standard requiring disclosure of actual achievement of the claimed therapeutic effect); and
- the fact that patentable second medical uses in Europe can even represent a selection from a broad prior art disclosure (such as treatment of a patient sub-group, or using a novel and inventive dosing regimen).

Possible FTO issues for innovators

Aside from likely difficulties in obtaining preliminary injunctions against "skinny label" generic products, there is another reason to believe that the appeal decision in the UK is not all good news for innovators.

This is because whilst the dispute in the *Warner-Lambert* case related to an *authorised* indication, there may well be other circumstances in which it is arguably foreseeable that a medicinal product will be dispensed for an ***unauthorised*** (but yet patented) indication.

Thus, unless and until the courts find reasons to dismiss the possibility of patent infringement in such circumstances, freedom-to-operate exercises for medicinal products marketed in the UK ought to address (at least in some way) all patents that are valid in the UK and that relate to medical uses of active ingredient(s) in the medicinal product.

Most worryingly, freedom-to-operate issues for a medicinal product could arise in respect of second medical use patents filed even after the product in question was first marketed. This is because it appears that infringement of such patents will not be judged upon the intentions of the party marketing the product, but upon the knowledge that they have (or ought to have) about the indications that the marketed product will ultimately be used to treat – including indications that are not mentioned on the product label.

Commentary and Action Points

If you have an interest in a medicinal product that is (or will be) marketed in Europe, you may wish to re-evaluate freedom-to-operate over second medical use patents relating to indications that are different from those on the product label. There may be a freedom-to-operate (or at least an infringement liability) issue in the UK if it is "reasonably foreseeable" that the product will be dispensed for a patented indication.

Alternatively, if you are planning to launch a new indication for an already marketed medicinal product, you may wish to consider (as discussed in the above-mentioned *Scrip Regulatory Affairs* article) developing a unique pharmaceutical form (or strength) for the new indication. In the light of the difficulty in obtaining preliminary injunctions against "skinny label" products, the use of such unique formulations may (especially if they discourage cross-label prescribing) represent the best option for maximising income from patented indications subsequent to expiry of all product *per se* patent protection.

Please contact Mike Snodin (at mike.snodin@parkgrove-ip.com) if you would like our advice on these or any other matters.