UK Skinny Label Infringement Litigation involving Pregabalin and Swiss Use Claims

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Background

- Pfizer (parent of Warner Lambert) markets LYRICA (pregabalin), approved for epilepsy, generalized anxiety disorder (GAD) and neuropathic pain.
- 2013 Sales of LYRICA in the UK were about $310 million, of which approx. 44% is thought to be for neuropathic pain.
    - 70% of 2014/2015 for pain
- Pfizer's patent protection for the pregabalin compound expired in 2013 and data protection expired in 2014
- Patent protection continues in Swiss use claim form directed to pregabalin for treating various types of pain.

Background (cont'd)

- Actavis (and other manufacturers) applied for marketing authorization for generic pregabalin, limited to epilepsy and GAD (the off patent indications)
- Actavis obtained marketing authorization and launch of its 'skinny label' version in the UK under the trade mark LECAENT. (in Feb 2015)
- Pfizer alleged that Actavis will infringe its pain patent.
- Actavis and Mylan also brought proceedings to revoke the pain patent.
- Sandoz sought approval for a 'full label' version of pregabalin
  - "On" and "Off" patent indications

UK Prescription Practices

- Where doctor's prescription specifies particular brand the pharmacist must dispense that brand.
- However, overwhelming majority of prescriptions are written by reference to the international non-proprietary name (INN) of the active ingredient.
- Prescriptions very rarely specify, and the dispensing pharmacist very rarely knows, the indication for which a drug has been prescribed.

More Background

- Actions taken to facilitate avoidance of mis-prescribing by healthcare bodies:
  - Actavis wrote over 7,500 pharmacists
  - Actavis wrote English clinical commissioning groups (CCGs)
  - Under Court order, NHS England issued guidance to CCGs advising LYRICA for pain
  - Software packages used by GPs in UK now updated to provide warnings of existence of patent rights when pregabalin prescribed for pain

Summary of UK Litigation

- Pfizer's interim injunction request denied (1/21/15 – Arnold)
  - No serious issue to be tried on direct or indirect infringement
  - Interpretation of Swiss-type use claim scope (not a product claim)
- Arnold J. refuses Actavis application to strike or dismiss direct infringement claim (2/6/15)
- Arnold J. grants Pfizer order compelling UK National Health Service to issue guidance (2/26/15)

Summary of UK Litigation (cont'd)

- Pfizer's appeal of injunction dismissed by COA (5/28/15 – Floyd)
  - Different interpretation of Swiss-type use claim
- High Court holds non-infringement (9/10/15-Arnold)
- Mixed decision on validity (insufficiency of some claims)
- Leave to appeal awarded on infringement (and validity) (10/15 – Arnold)
- Interim injunction restricting full label Sandoz granted (11/4/15-Arnold)
- Sandoz infringement and Actavis appeal decisions currently pending

Swiss Form Claims At Issue

- Claim 1: “Use of [pregabalin] or a pharmaceutically acceptable salt thereof for the preparation of a pharmaceutical composition for treating pain”
- Claims 3: “Use according to claim 1 wherein the pain is neuropathic pain”.

European Patent No. EP (UK) 0 934 061

English High Court Construction of Swiss Form Use Claims (Arnold J/Jan and Feb 2015)

- Claims at issue are process directed at manufacturer not doctor
- "Preparation" also includes packaging and labelling
- "For" means "suitable and intended for"
- The relevant intention is of the person who carries out the manufacturer of medicine

English High Construction of Swiss Form Use Claims (cont'd)

- Places burden on patent holders to prove subjective intent on the part of the manufacturer
- Interpretation of "for" also absolves downstream parties such as doctors and pharmacists from taking any steps to avoid providing a drug for a patented indication

Court of Appeal Decision (Floyd J/May 2015)

- It is sufficient for infringement that the producer knows, ought to know or could reasonably foresee that the medicine (in this instance) would ultimately be used for pain relief
- High Court's (Arnold J) test was too high
  - Requires patentee to show "wish or desire" to market for patented indication
  - "plain that Warner Lambert has an arguable case for infringement"

Issues considered in Court of Appeal Decision (Floyd J/May 2015)

- Sales figures of pregabalin for pain
- How is specific liability for patent infringement to be assessed?
- What sales can be considered infringing and which not?
- Even if assumed that a portion of Actavis sales would have gone to treat pain when it was sole generic, would this hold when there were other competitors?
- How should counter-action by Pfizer be factored into analysis?

Full Trial Decision (Arnold J/September 2015)

Non-infringement

- Manufacturer under ‘skinny label’ does not infringe a Swiss use claim stating a particular use of an off-patent drug
  - Downstream parties intentions relevant
- At no point in supply chain does a generic supplier or subsequent infringer (like a pharmacist) provide the drug knowing it will be used for the patented use (i.e. intentional infringement not foreseeable by Actavis
- Even if claims for all types of pain were valid, infringement was deminimis

Arnold J's Call for New System (para 722)

"I have reflected repeatedly and at length on the issues raised by this litigation. At the end of that period of reflection, I remain more convinced than ever that the best solution for the problem of protecting the monopoly conferred by a second medical use patent while allowing lawful generic competition of non-patented indications of the substance in question is to separate the patented market for the substance from the non-patented market by ensuring that prescribers write prescriptions for the patented indication by reference to the patentee's brand name and write prescriptions for the non-patented indications by reference to the generic name of the substance (the INN)"

Related Litigation: Warner Lambert v Sandoz (Full Label)

Interim Injunction Granted

- Evidence that pregabalin prescriptions referring to LYRICA were not at appropriate levels assuming pain accounts for 70% of market (relevant to irreparable harm)
- Risk that other full label pregabalin products could enter market with consequent price depression of LYRICA
- Rejected Sandoz's argument of no greater loss in light of skinny label approvals

Related Litigation: Warner-Lambert v. Sandoz (cont'd)

- Lloyds declined to stock skinny label products citing adverse event risks
- Arnold considered skinny label generic was not an unlicensed product and that off-label use was limited
- Since Pregabalin authorized for pain, it was held that there is no risk of pharmacist contravening regulatory law

Impact of Decisions and Business Considerations

- Arnold decision highlights actions taken by Actavis, Pfizer and health care bodies to avoid pain mis-dispensing
- To succeed in an infringement action involving a Swiss use claim, the patent holder must show the manufacturer knew, or at least it was reasonably foreseeable, that the generic medicine would be used for the patented indication
- How important were steps agreed to by Actavis to discourage infringing use relevant to decisions?

Impact of Decisions and Business Considerations (cont'd)

- What actions should a generic take to avoid infringement of Swiss-use claims?
- What risk-management steps can be put in place for a skinny-label scenario beyond patent law?
- Should a generic manufacturer communicate with pharmacies to make clear the indications for which label is approved?

Impact of Decisions and Business Considerations (cont'd)

- Would result be different if EPC 2000 claims ("substance X in use of treatment of Y") were used?
- Would "reasonably foreseeable" test be applied
- Is there any chance of Arnold J's solution becoming reality?
- More decisions and appeals in UK pregabalin case forthcoming!

Questions?