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Dosage Regimen Patent Held Invalid

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Last year, Actavis, Teva and Mylan ("Actavis") sought revocation in the English Patents Court of two patents relating to tadalafil, which is sold by Eli Lilly ("Lilly") as the active ingredient in CIALIS® to treat erectile dysfunction and pulmonary arterial hypertension. As is the usual course, ICOS (the patentee) and Lilly (the exclusive licensee) subsequently counterclaimed for infringement. At first instance, Birss J found the first patent in suit, EP (UK) 1 173 181, which concerned a dosing regime for tadalafil, to be valid and infringed and the second, EP (UK) 1 200 092, which concerned a specific formulation of tadalafil, to be invalid for lack of inventive step. However, Birss J granted Actavis leave to appeal his decision on EP 181 (only). On 1 November 2017 Kitchin, Floyd and Lewison LJJ overturned Birss J's decision on inventive step. Unusually, all three judges, each of whom has substantive patent law experience, gave a judgment which is contrary to the standard practice of one judge writing the decision and the two others agreeing.

In giving the leading judgment, Kitchin LJ carefully considered Birss J's analysis of construction (pausing to note that the Supreme Court's decision in **Actavis v Lilly** was not relevant), priority, added matter, novelty and obviousness. He (together with Floyd and Lewison LJJ) agreed with Birss J in all respects on each of these issues other than obviousness. With regard to obviousness, the key question in issue was whether it was obvious to the skilled person, in light of a piece of prior art called Daugan, that a 5mg daily dose of tadalafil would be a safe and effective treatment for sexual dysfunction with minimal side effects.

Daugan disclosed tadalafil as being an effective inhibitor of PDE5, the appropriate enzyme for sexual dysfunction, and tadalafil tablets at a dose of 50mg per day. Partially using the well-known analysis of Kitchin J in **Generics v Lundbeck** [2007], Birss J had stepped through a checklist of factors and found that, based on Daugan, a 5mg dose of tadalafil would not have been tested by the skilled team with a reasonable expectation of success and therefore that the 5mg dose in EP 181 was not obvious. However, the Court of Appeal disagreed with Birss J (despite his use of the **Generics v Lundbeck** list) explaining that the expectation of success in relation to the efficacy of a 5mg dose was irrelevant because it was very likely that a 5mg dose would have been investigated as a matter of routine. Kitchin LJ further explained that ascertaining the relationship between dose and efficacy is the purpose of a routine Phase IIb clinical study. The Judge considered that, in light of Daugan, the skilled person would embark upon carrying out routine pre-clinical and clinical trials with tadalafil for sexual dysfunction with a reasonable expectation of success. In the course of doing so, they would carry out Phase IIb dose ranging studies with the aim of finding out the dose response relationship. As a result of those studies they would very likely test the 5mg per day dose and, if they did so, would find it to be safe and efficacious.

The tadalafil decision is interesting, not least because it is rare for the Court of Appeal to overturn a first instance decision on the issue of inventive step. Kitchin LJ was keen to emphasise that the Court was not ruling that dosage regimens could never be inventive, but rather that this particular patent was at the end of a process that a skilled but non-inventive team would embark upon with a reasonable expectation of success. The decision is also of interest with regard to so-called 'bonus' effects. In his short judgment, Floyd LJ expressed the view that the skilled team would not have been able to predict that the lower dose of 5mg would be effective. However, in Floyd LJ's view, this was not the correct way to evaluate the issue. Rather the correct analysis was that if, as the trial judge had held, the findings in relation to 5mg would be arrived at by standard, routine enquiries into dose response, the surprising result did not make such routine enquiries inventive.

It is not known whether Eli Lilly will seek to obtain permission to appeal from the Supreme Court.

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