PATENT WATCH


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Eli Lilly wins Alzheimer's antibody patent dispute

A court in the United Kingdom has ruled that one of Janssen's patents that protected the flunked Alzheimer's disease therapy bapineuzumab is invalid. This was because the court held that the antibody drug was not adequately described in the patent. If the bapineuzumab patent had been valid, Eli Lilly's solanezumab — which is currently in late-stage clinical trials — would have infringed on the bapineuzumab patent.

Janssen's patent (EP(UK)1 994 937) claimed an "antibody directed to amyloid-β that is useful for preventing or treating a disease that is characterized by amyloid deposit in a patient".

When amyloid precursor protein is cleaved by β- and γ-secretase enzymes, amyloid-β peptides are created, which can then form the plaques that are characteristic of Alzheimer's disease. Antibodies against the amyloid-β peptides — such as solanezumab and bapineuzumab — are thought to induce an Fc-mediated immune response in the brain to clear amyloid-β. Although both antibodies work via the same mechanism, solanezumab targets a middle portion of amyloid-β, whereas bapineuzumab targets an amino-terminal fragment.

Lilly sought to revoke the patent on several grounds, including insufficiency, meaning that the patent did not describe the invention (that is, bapineuzumab) in sufficient detail to enable a skilled person to carry out the invention without undue burden. The court determined that the patent lacked sufficiency from two angles.

First, it highlighted that the claims were overly broad; namely, the patent did not limit the invention to antibodies that targeted a specific portion of amyloid-β (for example, N-terminal fragments). Because of this omission, other skilled people would be presented with a "conundrum of which tests to rely" to achieve the invention and have a high prospect of failure.

Second, the court held that Janssen did not succeed in making an antibody that could achieve the therapeutic effect described in the patent — namely, for preventing or treating a disease characterized by amyloid deposits in a patient. Here, the court found no evidence — such as results from mouse cognition tests — that would allow a skilled person to predict that the reduction in amyloid-β levels induced by bapineuzumab would lead to cognitive benefit in patients. Notably, the court noted that the failure of bapineuzumab to meet its primary end points (based on cognition scores) in a recent Phase III clinical trial added further evidence to show that the claim was not achieved.

Although Eli Lilly's solanezumab also missed its primary end points in a pivotal Phase III trial, it slowed cognitive decline in patients with mild Alzheimer's disease and so is undergoing further testing in this patient population as well as in several prevention trials (see *Nature Rev. Drug Discov.* **11**, 657–660; 2012).

Janssen can appeal the decision.

Teva loses key MS drug patent

Teva has seen several claims in patents protecting its innovator multiple sclerosis (MS) drug Copaxone (glatiramer acetate) knocked down by a US appeals court. The ruling means that Teva could face generic competition for the US$4-billion-a-year drug 16 months earlier than previously expected.

Teva owned nine patents that protected Copaxone and methods of making it, which were challenged by Mylan and Sandoz. Copaxone is a polymer (sometimes called copolymer-1) that is made up of the amino acids alanine, glutamic acid, lysine and tyrosine in a specific ratio. Because a sample of Copaxone typically consists of a mixture of individual polymer molecules that have differing molecular masses, there are several ways to describe the resulting distribution of molecular mass values.


Huw Jones/Alamy

It was this that the challenge was based on; that is, the description of the molecular mass of Copaxone in some of the claims was ambiguous. For some claims, Teva had described molecular mass based on how many molecules in a sample have molecular masses that fall within a set range, such as "copolymer-1 having over 75% of its mole fraction within the molecular weight range from about 2 kDa to about 20 kDa". And the court said this language was not ambiguous.

But for other claims, Teva had used the wording "copolymer-1 having a molecular weight of about 5 to 9 kDa". The court said this wording was ambiguous because the average molecular mass could be calculated in several ways, such as the arithmetic mean, the molecular mass of the most abundant molecule in the sample or the mass average molecular mass, and these measurements can each have different values for a typical polymer.

Although Copaxone still has patent protection based on the non-ambiguous claims until 2014, the longest-lasting patent that was due to expire in 2015 (US 5800808) has been lost, meaning that generic competition could begin in 2014. However, the US Food and Drug Administration has not yet approved generic versions of glatiramer acetate. In addition, Teva is hoping to receive regulatory approval for its alternative form of Copaxone (a higher dose with fewer injections), which is anticipated to have patent protection until 2030.

The requirement of a detailed description of the molecular mass of Copaxone in order for the claims to be valid in the current case was consistent with the outcome of a recent case in the United Kingdom. In that case, Teva's claims to Copaxone described the number of molecules in a sample that had molecular masses within a set range, and these claims were found to be non-ambiguous.

A longer patent life for formulated drugs in Australia?

Drugs that are formulated to improve their therapeutic characteristics — such as controlled-release formulations — may be