Humira®: recent developments

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The world's top selling drug adalimumab (Humira®) produced revenues of \$16.0 billion for AbbVie (Chicago, IL, USA) in 2016. However, its position is coming under challenge. We recently highlighted the history of the drug and the challenges it was facing [1]. A number of recent developments make it worth revisiting this issue.

Biosimilar developments

Year 2016 saw the first approval of an adalimumab biosimilar when the US FDA approved Amjevita (Amgen®, CA, USA) on 23 September, approving it for all the same indications as Humira. However, Amjevita has yet to be launched because of ongoing patent litigation between Amgen and AbbVie.

In January 2017, the EMA's Committee for Human Medicinal Products recommended approval of Amgen's adalimumab biosimilar as both Amgevita and Solymbic, the latter having a slightly more restricted label [2]. Formal EU approval should be forthcoming in late March. As of February 2017, the EMA also had two other adalimumab biosimilars under review.

Patent litigation

The primary product patent for adalimumab expired at the end of 2016 in the USA and expires in October 2018 in Europe but AbbVie has developed a large portfolio of secondary patents which it claims offers protection until

at least 2022. Unsurprisingly these have come under challenge as we discussed previously [1].

In February 2017, Samsung Bioepis® (Incheon, South Korea), its partner Biogen Idec® (Cambridge MA, USA) and Fujifilm Kyowa Kirin Biologics (Tokyo, Japan) succeeded in their action to invalidate certain AbbVie's secondary patents [3]. In the Patents Court of the High Court of England and Wales, the judge ruled that AbbVie was not entitled to claim the priority dates that it had for the method of use patents EP-1944322; and EP-2940044 [4,5]. Although this ruling only invalidates AbbVie's patents in the UK, it is anticipated that it will precede with similar actions and patent revocations elsewhere in Europe.

In the USA, the position is more complicated with both patent litigation and multiple intra partes reviews (IPR) going on. To date AbbVie has had a degree of success in winning IPR challenges but further IPRs have then been filed. In January 2017, Coherus Bio-Sciences™ (CA, USA) filed four petitions seeking to overturn US-9085619 [6] and followed this with two more in March 2017. In November 2016, it had failed to get a review of its petition to overturn US-9114166 [7]. Coherus has outstanding IPRs against other AbbVie patents as does Boehringer Ingelheim (Ingelheim, Germany). US-8889135 [8] is the subject of two IPRs from Boehringer and one

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from Coherus. Coherus also has an outstanding IPR against US-9073987 [9].

“By the time that issue is resolved, other companies can be expected also to have obtained FDA approval for the marketing for adalimumab biosimilars.”

On 4 August 2016, AbbVie filed a patent infringement suit, in the District Court of Delaware, against Amgen claiming that the latter's Biological License Application filing infringed ten AbbVie patents [10]. These patents were identified as part of the ‘patent dance’ defined under the Biosimilar Price Competition and Innovation Act, which involves the applicant (Amgen) submitting a copy of its license application to the existing licence holder showing which patents are not infringed. Until this case is resolved Amgen cannot launch Amjevita, except by risking further litigation. The two parties have filed initial depositions but no trial date has yet been set. These initial depositions highlight the patents that are claimed to be infringed as covering processes for the production of adalimumab [11–14], its formulations [15–18] and therapeutic methods of using it [19,20].

None of these ten identified patents correspond to those being challenged by the IPRs filed by Coherus or Boehringer Ingelheim. A total of 14 AbbVie patents related to adalimumab are currently under challenge in the US patent and legal systems.

Conclusion

It is unsurprising, given the high proportion of AbbVie's revenues that it generates that AbbVie is seeking to defend adalimumab revenues with an extensive patent portfolio. Although primary patent protection has expired in the USA, it appears more likely that adalimumab biosimilars will be launched in Europe before they are in the USA. The recent High Court ruling in the UK that has invalidated certain key patents in the UK is likely to be followed by similar litigation, but not necessarily the same outcome in Germany, France, Italy and Spain. In contrast, in the USA, developments will be heavily influenced by the Patent Office's rulings on the IPR challenges since these can be expected to be resolved well before the outcome of the litigation between Amgen and AbbVie. By the time that issue is resolved, other companies can be expected also to have obtained FDA approval for the marketing for adalimumab biosimilars. Thus, patent litigation will have a major impact upon the long-term revenue prospects of the world's best selling drug.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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