The Pemetrexed Pendulum Swings Back

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Pemetrexed, yet again: last Wednesday the District Court of The Hague, swimming against the current and after a deep dive in the prosecution file, decided that Fresenius did not infringe Eli Lilly's 'pemetrexed disodium' patent with a generic product that does not contain pemetrexed disodium, not even by equivalence.
The basic facts of the widespread Pemetrexed litigation will be well-known to most readers by now. Eli Lilly's patent (EP 1 313 508) has a Swiss form claim relating to the "use of pemetrexed disodium" in combination with vitamin B12 for inhibiting tumor growth. Different generic companies do not use pemetrexed disodium in their product, but another form of pemetrexed (e.g. pemetrexed diacid, as in Fresenius' product). Do these generic products fall within the scope of Lilly's 'pemetrexed disodium' claim?

That question was put before numerous European patent judges over the past years. For a walk down memory lane, just skim the reports on this blog. Or, to list a few decisions:

Netherlands			
March 1, 2017	District Court (summary proceedings)	Lilly/Sandoz	Patent valid and infringed (no non-infringement defense)
October 24, 2017	District Court (summary proceedings)	Lilly/Teva	Patent infringed (no invalidity defense)
October 24, 2017	District Court (summary proceedings)	Lilly/Fresenius	Patent infringed
May 8, 2018	Court of Appeal (summary proceedings)	Teva/Lilly	Patent infringed
May 8, 2018	Court of Appeal (summary proceedings)	Fresenius/Lilly	Patent infringed
January 16, 2019	District Court (merits proceedings)	Sandoz/Lilly	Patent held valid (invalidity action only)
United Kingdom			
May 15, 2014	High Court	Lilly/Actavis	No infringement; DNI granted
June 25, 2015	Court of Appeal	Lilly/Actavis	DNI direct infringement confirmed, contributory infringement not
July 12, 2017	Supreme Court	Lilly/Actavis	Patent infringed
Germany			
April 3, 2014	Landgericht Düsseldorf	Lilly/Actavis	Patent infringed
March 5, 2015	Oberlandesgericht Düsseldorf	Lilly/Actavis	No infringement
June 14, 2016	Bundesgerichtshof	Lilly/Actavis	Incorrect application equivalence doctrine; remitted.
June 24, 2016	Landgericht München	Lilly/Ratiopharm	Patent infringed
May 18, 2017	Oberlandesgericht München	Lilly/Ratiopharm	Patent infringed
July 17, 2018	Bundespatentgericht	Hexal and Stada/Lilly	Patent invalid
Italy			
September 10, 2017	Tribunale Ordinari di Milano	Fresenius/Lilly	No infringement; DNI granted
October 15, 2018	Tribunale di Milano	Fresenius/Lilly	Patent infringed; DNI denied
Switzerland			
March 9, 2017	Bundespatentgericht	Actavis/Lilly	DNI granted
October 20, 2017	Bundesgericht	Lilly/Actavis	Patent infringed (one product); remitted for two other products
December 21, 2017	Bundespatentgericht	Actavis/Lilly	Patent infringed two other products

And to list some more: Denmark (8 December 2017: injunction granted against Fresenius); Austria (22 December 2017: injunction granted against Fresenius; 12 April 2018 injunction confirmed on appeal); Finland (29 December 2017, injunction granted against Actavis and Ratiopharm); Sweden (31 January 2018, injunction granted against Actavis), Belgium (15 June 2018: injunction against Fresenius denied; no infringement)…everyone seems to have gotten a piece of the pemetrexed pie.

Well aware of this (then shorter) cascade of decisions, The Hague Preliminary Relief Judge wrote in his 24 October 2017 judgment:

> *The Preliminary Relief Judge's opinion that there is an infringement, is supported by a number of important foreign judges […]. However, some other foreign judges have not accepted infringement. This is mainly due to a different valuation of the prosecution file and how strictly one adheres to the precise wording of the claims. These divergent decisions, moreover, underline once again the desirability of the Unified Patent Court (UPC), whereby one common judgment can be reached for a very large number of countries in Europe.*

Wednesday's decision of the District Court confirms that different judges can come to different decisions, also in the Netherlands. Other than the Preliminary Relief Judge, and on appeal The Hague Court of Appeal, the District Court did *not* find infringement.

The Protocol and points of view to consider

The court starts with a familiar mantra: "The scope of protection of a European Patent is, on the basis of Article 69 of the European Patent Convention, determined by the claims, where the description and drawings serve to interpret the claims." And, familiar to all, that Article 1 of the Protocol prescribes that an interpretation of the claims should be found between two extremes: on the one end a strict, literal meaning of the wording used in the claims, and on the other end the claims only serving as a guideline and that the actual protection conferred may extend to what, from a consideration of the description and drawings by the skilled person, the patent proprietor has contemplated. And, of course, that Article 2 Protocol prescribes that due account shall be taken of any element which is equivalent to an element specified in the claims.

The court continues with discussing how this how-to interpret article 69 EPC has been intepreted by the Dutch Supreme Court and lower courts over the years:

- The inventive concept behind the wording of the claims is a 'point of view' opposite to then strict, literal meaning of the wording of the claims (in the Protocol's words: the extremes).
- Parties agree the one extreme (literal meaning of the claims) is limited to the use of pemetrexed disodium, while the other extreme (the inventive concept) is not limited to pemetrexed disodium.
- The skilled person is aware that the literal meaning of the claims is a limitation with respect to the inventive concept (knowing that the activity of the combination therapy with vitamin B12 is not specific to pemetrexed disodium, but can also be achieved with other forms of pemetrexed).
- The question to be answered is how to find the middle position between the two extreme interpretations.
- The point of view of the inventive concept does not yet provide any indications how to find a position between a fair protection for the patent proprietor with a reasonable degree of legal certainty for third parties.
- The court has to consider if the result of its assessment provides the reasonable degree of certainty to third parties. That point of view can result in a more restrictive interpretation of the claims (in line with their literal wording), i.e. due to a lack of clarity of the claims works against the patentee.
- Another point of view to consider is the degree of innovation an invention has brought.
- Yet another point of view is if – according to the skilled person – the scope of protection has consciously been limited by the patentee. In that regard the skilled person's answer to the question if there were 'good reasons' for a limitation can be taken into account.

Limitation of the inventive concept: more than technical reasons

The District Court points out that the Court of Appeal (in the 2018 summary proceedings) considered that a 'conscious choice' must be understood as a 'conscious choice based on a technical reason'. There should be 'technical considerations' knowable to the skilled person to come to a more limited interpretation of the claims than the inventive concept entitles, according to the Court of Appeal. The Court of Appeal considered that none of the points of view indicate that third parties could have assumed that Lilly has consciously chosen pemetrexed disodium for a technical reason.

The District Court does not agree: if there is not a known, conscious technical reason for a limitation in the wording of the claims (compared to the inventive concept), then this does not mean that the skilled person should always assume that this limitation should (therefore) not be considered a limitation of the scope of protection. Other circumstances and points of view can still play a role. For example, a lack of clarity as to the contents c.q. scope of the claims works against the patentee. On the other hand, if the limitation is not based on conscious decision (if the limitation is clearly unintended), this speaks for a wider scope of protection.

The prosecution file

The District then comes to a decisive factor for this case: the prosecution file. In line with Supreme Court case law, the District Court notes that the prosecution file should only be restrictively used for arguments in favor of the patentee (i.e. only to a limited extent in case the skilled person can reasonably have doubts about the meaning of the claims after having studied the description and drawings). This is in line with the prescribed reasonable degree of legal certainty for third parties. The legal certainty does not provide any limitation if a third party wants to rely on the public part of the prosecution file to substantiate its interpretation of the claims. The court subtly notes that this "different from what seems to be thought" in other European

countries (referring in a footnote to par. 84 of the UK Supreme Court's 12 July 2017 judgment).

The court is of the opinion "that, given the nature of the limitation and the manner in which that limitation took place according to the prosecution file, the skilled person (at least: the third party) will not regard the literal wording of the claims as a (clearly) unintended limitation".

In short, the court considers that:

- Lilly replaced 'an antifolate' in the original application with 'pemetrexed' after the examiner raised objections (i.a novelty).
- The examiner subsequently raised an added matter objection as to the use of the term 'pemetrexed', noting that this term in the wording of the claims and the description "is certainly a distinct compound [follows the CAS number for pemetrexed diacid] of the 'premetexed disodium' [follows the CAS number for pemetrexed disodium]" as expressed in the original application.
- The skilled person would have understood that with the term 'pemetrexed' Lilly meant to refer to the antifolate (the pemetrexed anion), and not the specific diacid. This follows from the inventive concept disclosed in in the original application, and is also a logical conclusion in view of Lilly's amendment of 'antifolate' into 'pemetrexed'.
- The court considers that Lilly – in these merits proceedings – is also of the opinion that the application did provide basis for a claim with a wider scope than the current claim.
- As to the amendment into pemetrexed the examiner did not say that the application did not provide basis for pemetrexed disodium only. The skilled person would have derived from the Examiner's communication that the examiner's reference to pemetrexed concerned the diacid (and not the anion), and that the examiner had misunderstood Lilly.
- Lilly did not take any step to communicate that its use of pemetrexed was *not* meant to specifically refer to the diacid, buth the antifolate pemetrexed (with the active anion). Instead, Lilly amended its claims to pemetrexed disodium. That while it was foreseeable at the priority date that there were other pharmaceutical dosage forms of pemetrexed, which were in the skilled person's reach. Lilly accepted without objection that the examiner thereafter limited the description to only pemetrexed disodium.

The skilled person, having reviewed the prosecution file and then having read the claims and description, can only conclude that scope of the claim is limited to use of pemetrexed disodium. The court adds that a "pharmaceutical superpower" as Lilly has the necessary expertise and experience in filing patent applications, while there was no time pressure on the examination proceedings. This supports that Lilly deliberately limited the claims to pemetrexed disodium (which Lilly also did not deny). That there was no technical reason for the limitation is – in view of Lilly's deliberate choice – insufficient to decide in Lilly's favour. Any lack of clarity comes for Lilly's account.

Pemetrexed Fresenius therefore does not fall within the patent's scope of protection, according to the court. The court notes that it has taken due account of equivalence when determining the middle between the Protocol's extremes. The court's assessment does not leave room for the protection of (also) other dosage forms of the antifolate pemetrexed.

More equivalence

The court's decision was based on the assumption that the original application did provide basis for other pemetrexed forms than pemetrexed disodium. As an *obiter* the court considers that its decision would not have been different if it should be assumed – other than the parties did – that there was no such basis in the application. In that case, dosage forms equivalent to pemetrexed disodium were still in the skilled person's reach at the priority date while Lilly did not provide a basis for these other forms in the application. That could not have been clearly unintended. Lilly did not state that the application contained an error or omission, and it does also not follow from Lilly's limitation to pemetrexed disodium – without discussion – during the examination proceedings.

Finishing up on equivalence, the court adopts Arnold J's consideration in his 2014 UK pemetrexed decision that patentees resort to arguments about equivalents in three main classes of cases. The reader who is still reading at this point will be able to look up what these three classes are (see par. 104 – 107 of Arnold J's decision). Let's limit the wording here to this: according to the District Court this was not one of the first two cases (in which "it can be fair that equivalent protection has a corrective effect"). And in the third class of case there is, Arnold J's words, "no reason why the law should be sympathetic to the patentee". Sympathetic the law – as applied by the District Court – was not for Lilly: "an appeal for protection according to equivalence is not meant to reverse Lilly's in hindsight unwelcome choices in the wording of its patent at the cost of the reasonable degree of legal certainty for third parties."

The District Court's decision and reasoning is a welcome addition to the continued discussion on claim construction, if and how the prosecution history should aid this construction, and what part equivalence should play in all of this. As to the latter, reading this decision raises the question: will equivalence swing back again with the pemetrexed pendulum?

The 19 June 2019 of The Hague District Court is available here (in Dutch).