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NL – Cinacalcet patent held invalid and SPC null

Boukje van der Maazen (Brinkhof) · Friday, March 1st, 2019

In nullity proceedings initiated by Accord Healthcare ("Accord") the District Court of The Hague has held Shire-NPS Pharmaceuticals' ("NPS") patent EP 1 203 761, the basic patent for an SPC covering cinacalcet, invalid for lack of inventive step and declared the SPC null. In short, the court considered that the (selection of) cinacalcet provided no technical contribution to the prior art, while the skilled person would have selected cinacalcet with a try-and-see approach.

Selection invention: assessment of inventive step

EP 761 relates to a selection invention. The compound cinacalcet was selected from a class of calcimimetic compounds already disclosed in three prior art documents (WO 373, WO 959 and US 827).

Both Accord and NPS referred to the Guidelines for Examination of the EPO (Part G, Chapter VII, below 12.) and the Annex thereto (idem, below 3.1) for the relevant test for assessing inventive step in selection inventions. The court follows the parties in this approach and summarizes the test as follows:

1. *Does cinacalcet provide a technical contribution to the prior art, i.e. does the selection possess unexpected advantageous or improved properties over the prior art?*

   No? No inventive step.

   Yes? The following question has to be asked:

2. *Would the skilled person have made the selection from the prior art hoping to solve the underlying technical problem or expecting to find the advantageous or improved properties?*

   If so, there is no inventive step.

Ad 1) Unexpected advantageous or improved properties over the prior art?

NPS argued that cinacalcet has unexpected advantageous/improved properties over prior art compositions in terms of (the combination of) calcimimetic activity, toxicity and bioavailability.

As for the favourable toxicity and bioavailability NPS relied on post-published evidence. According to NPS this post-published evidence could be taken into account because the technical

effect of cinacalcet's suitability as a drug (which includes favourable toxicity and bioavailability) had been made plausible in *the patent*. The court rejects this argument as the claimed technical effect should be made plausible *in the original application*. In this case, the original application provided a basis for cinacalcet's calcimimetic activity, but not for its toxicity and bioavailability. NPS could therefore not rely on any post-published evidence that show such technical effects.

NPS further argued that the calcimimetic activity of cinacalcet was unexpectedly high. NPS relied on a table in the patent to illustrate that the calcimimetic activity is higher than the most active composition known in the prior art.

According to the court, an improved activity is as such not sufficient to be considered an unexpected advantageous property. The prior art already mentioned that other compounds could be screened in order to determine other useful lead molecules, which naturally may also have a higher activity than the already disclosed compounds. Also the original application did not disclose that cinacalcet's activity is extraordinary for its class.

Therefore, the court holds that cinacalcet does not make a technical contribution to the prior art.

Ad 2) Would the skilled person have made the selection?

Still, the court considers the second question and concludes that the patent *also* lacks inventive step because the skilled person would have made the selection.

Here the party debate focused on the question whether the skilled person would adopt a "try-and-see" attitude when screening compounds for a higher activity. The court considers in line with TBA case law that the requirements for accepting a reasonable expectation of success are less demanding if:

1. the prior art directs the skilled person to certain further research;
2. and the skilled person could carry out that research by routine experiments.

Dutch decisions discussing a try-and-see situation are scarce. In a 29 June 2016 decision in proceedings between MSD and Ono on pembrolizumab, the District Court rejected MSD's reliance on a try-and-see situation, as a prior art document would discourage the skilled person to carry out routine tests. In a 26 October 2016 decision in proceedings between Actelion and Icos on tadalafil, the District Court *did* conclude that the skilled person would adopt a neutral try-and-see attitude. Finally, in a 31 October 2017 decision in proceedings between Sandoz and AstraZenca on fulvestrant, the Court of Appeal The Hague rejected Sandoz' argument that the skilled person would adopt a neutral try-and-see attitude. According to the Court of Appeal such an approach to inventive step would mean a departure from the (strict) condition that an invention only is obvious when the skilled person *would* (and not only *could*) have arrived at the invention on the priority date.

Accord argued that the skilled person would adopt a neutral try-and-see attitude, because routine testing suffices to determine which of the compounds within the general formula possesses a higher activity than the most active compound from the prior art. Moreover, the prior art explicitly invites the skilled person to do such further testing.

The court follows this line of argumentation. As the prior art encourages the skilled person to do research to find other suitable calcimimetic molecules, the skilled person would not be discouraged

by the size and extent of the research (contrary to the above referred to Sandoz/AstraZeneca case where such a *pointer* was lacking). Also the fact that the general formula disclosed in the prior art comprises a large number of molecules would not discourage the skilled person in his attempt to find other compounds. Therefore, the skilled person would have made the selection and the patent is also under the second question not inventive.

The District Court's 6 February 2019 decision is available here (in Dutch).

Disclaimer: the author's firm acted for Accord.

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