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Orion's Three-In-One Formulation Patent for Entacapone, Levodopa and Carbidopa Declared Null by the Belgian Courts

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On May 9, 2017, the Dutch-speaking Brussels court of commerce handed down its decision on the merits in the context of an infringement action initiated by Orion and its exclusive licensee Novartis against Belgian generic company Eurogenerics.

The proceedings relate to Orion's European patent EP 1 189 608, concerning an oral three-in-one solid composition of entacapone, levodopa and carbidopa, wherein a substantial portion of carbidopa is separated from entacapone and levodopa. On the basis of EP '608, Novartis commercializes the medicinal product Stalevo® used in the treatment of Parkinson's disease. Eurogenerics obtained a marketing authorization for an alternative three-in-one formulation of entacapone/levodopa/carbidopa using Stalevo® as reference medicinal product. Novartis considers that the generic product of Eurogenerics falls under the scope of protection of EP '608 and therefore initiated an infringement action, based on either a literal infringement or an infringement by equivalence.

Although Eurogenerics contested the infringement of EP '608, it challenged its validity by way of a counterclaim. The request for a preliminary injunction ("PI") was dismissed for a lack of prima facie infringement in the decision of 20 May 2015 of the President of the Dutch-speaking court of commerce. The PI was also dismissed at appeal, albeit for a lack of a prima facie valid patent. For this important change in Belgian case law related to the prima facie validity of European patents, we refer to previous blog entries (link and link).

Eurogenerics has now also prevailed in the proceedings on the merits.

The Brussels court of commerce confirmed that EP '608 is invalid due to a lack of inventive step applying the problem-solution approach. As the combination of entacapone, levodopa and carbidopa was already disclosed in the prior art, in particular in one of Orion's earlier patents, only the separation of carbidopa from the other two active substances claimed in EP '608 had to be assessed on its validity. The court noted in this regard that the separation of active substances was part of the prior art. The fact that such separation was only carried out when strictly necessary, does not imply that this process was exceptional, new or inventive. Considering the known chemical instability between levodopa, carbidopa and entacapone, a skilled person would have a clear incentive to separate one of the active substances in order to guarantee (and maintain) the chemical stability of the three-in-one formulation.

Even the selection of carbidopa as the substance to be separated from the other active substances was not inventive, in casu excluding carbidopa from the joint granulation process of entacapone and levodopa. Orion and Novartis indeed confirmed during the proceedings that the size of the resulting three-in-one tablet (and its stability) was an actual concern. As a granulate mixture has several advantages (e.g., less segregation, more easily to compact/compress), the skilled person would have found it obvious to opt for the separation of carbidopa from the granulation process – being the smallest fraction in the total weight ratio of the formulation – and adding it afterwards to a granulate mixture comprising levodopa and entacapone with its inherent beneficial characteristics. Only this process would have resulted in the most compact and stable tablet.

Finally, as the separation of carbidopa was an obvious choice, the court considered that any alleged unexpected therapeutic efficacy resulting from this separation could not render the invention inventive.

Given the absence of a valid patent (at least as regards the invoked claims 1, 2, 22 and 23 of EP ‘608), Eurogenerics could not infringe the invoked patent rights of Orion and Novartis.

The discussed decision is known as court of commerce of Brussels (Dutch-speaking – 5th Chamber), Orion-Novartis / Eurogenerics, 9 May 2017, n° A/15/04306.

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