4412- Valsartan-saccubitril- cocrystal- a round up

Finally, the judgement from the Patent office on valsartan-saccubitril co-crystal is out. Just to put things in perspective, Novartis had filed a patent application for a co-crystal or supramolecular complex (SMC) of valsartan and saccubitril – 4412/delNP/2007. The Application was examined and opposed by 8 opponents including Natco and Indian Pharmaceutical Alliance. Hearings were held between May 21 to September 21. Thereafter, the matter reached the doors of the High Court of Delhi in a writ petition filed by Natco regarding cross-examination of experts. The High Court gave directions to the Controller to conduct the hearings expeditiously and pronounce judgement by November 15, 2022.

Thereafter, the Controller expeditiously conducted hearings and eventually now, the Controller has granted patent no. 414518 in favour of Novartis.

What follows is a brief review of the order- though this is worth a thesis. One of the main grounds of opposition was anticipation – that the co-crystal as claimed was anticipated by WO2003/059345 – that this document clearly teaches a combination of Valsartan and sacubitril and the co-crystal was anticipated by this document. The Controller holds that WO345 is a patent application disclosing a physical mixture and there is no disclosure of the co-crystal- hence no case of anticipation is made out. So far good. But he also holds that "it is not easily predictable" that supramolecular complexes may be formed and properties of such complexes cannot be anticipated from WO345. Besides, the Controller also finds that there is no enabling disclosure of a complex in WO345.

While the Controller may not have found actual verbatim description of an SMC in WO345, and without getting into the nuances of interpretation of WO345, clearly, the finding on predictability is outside the realm of anticipation. Lack of novelty is an objective approach- with no scope for 'predictions' based on prior art.

The next ground taken by some of the Opponents was of prior claiming – that the claims of the SMC were prior claimed by WO345. Prior claiming, as we know is a claim-to-claim comparison. In fact, WO345 being a foreign publication does not even qualify for prior claiming. However, the Controller makes no finding on that count. He however, rejects this ground on the premise that the subject matter of claimed invention is different from WO345. Totally missed the point on law.

The ground of obviousness was taken by almost every opponent. The premise was that WO345 already taught combination of valsartan and sacubitril and there were prior art that taught preparation of co-crystals of different drugs, the properties thereof were known and therefore it was obvious to prepare co-crystal of valsartan and sacubitril. Here the Controller first analyses each prior art individually- which is entirely against the basic tenet of obviousness. Lack of inventive step is primarily based on a mosaic of prior art- that the prior art as a combination teaches or leads to the claimed invention. However, an analysis of each document is painstakingly undertaken and but naturally, the conclusion from each document would be that these individually do not teach the co-crystal of valsartan and sacubitril. Yes they don't and it wasn't even argued.

He then attempts a combination of the prior art – and concludes based on his findings on each individual document that each of them do not teach co-crystal, the claimed invention is not obvious. He concludes that innumerable modifications are to be made to the prior art WO345 or other art to arrive at the co-crystal. There is no finding on the effect of collective wisdom of the prior art- To be fair the Controller finds that a significant number of experiments would have to be conducted by a POSA to arrive at cocrystals - the point is – after 30 odd years of scientists working on polymorphs and co-crystals day-in and out, is this sufficient reason for a finding of non-obviousness?

As for 3(d) the Controller relies on various post-filing articles cited by the Applicant to find that LCZ696 (SMC) is superior to monotherapy, that LCZ696 is a breakthrough product, and that LCZ696 was tested against valsartan for reduction in blood pressure. Reliance is also placed on an article by Rouilope wherein LCZ696 is compared with physical combination of valsartan and sacubitril. In my personal view, the Controller ought not to have relied on any of these articles – for the simple reason that they are post-filing. If this therapeutic effect is fundamental to the invention, it should have found place in the patent specification.

The ground of insufficiency is also found in favour of Novartis- as the Controller finds that the specification not only discloses the preferred embodiment but all the disclosures fulfilling section 10(4) are found in the specification. In a way, this finding is not wrong. But it is also true that the claim is not enabled for the entire range of the claim. There is no finding on that account, and that was the argument made by the Opponents.

After most of the hearings concluded on 3rd November, two further pre-grant oppositions were filed by Hemavathi and Dr Kanchan Kohli. Both stand rejected by the Controller since the prior art and grounds relied upon by them are similar to that raised in previous oppositions. As such the Controller found that the oppositions were not in aid of examination and rejected them. I believe this may be one of the few decisions wherein such a bold action has been taken.

This is one of the few cases wherein multiple oppositions had been filed and it took almost 4 years for the Controller to wade through the ocean of oppositions and conclude the matter. Considering that the time constraints and the amount of pleadings before the Controller, the order is the result of burning the midnight oil over several nights. But being such an important product, our expectations are far higher.

I would be surprised if there are no challenges to this order in the High Court.