(2013) 05 IPAB CK 0006

In the Intellectual Property Appellate Board

Case No : M.P. No. 12/2011, 13/2011 In OA/14/2011/PT/DEL

Euro-Celtique SA — APPELLANT

Vs

Assistant Controller of Patents And Designs — RESPONDENT

Date of Decision : 02-05-2013

Acts Referred:
Patents Act, 1970 — Section 2(1)(g), 3(d), 3(e), 8, 10(4)

Citation : (2013) 05 IPAB CK 0006

Hon'ble Judges : Prabha Sridevan, J;D.P.S. Parmar, Technical Member

Bench : Division Bench

Advocate : Archana Shanker, Neeti Wilson

Final Decision : Dismissed

Judgement

Prabha Sridevan, J

1. The invention in patent application No. 6117/DELNP/2007 is for a ""Dosage Form Containing Oxycodone and Naloxone"". The Controller held that

the application does not meet the requirements of Section 2(1)(g), 3(d), 3(e), 8 and 10(4) of the Patents Act. He relied on five prior arts:

D1: WO 2003/084504

D2: WO 2003/007802

D3: WO 2002/092060

D4: DE 4325465

D5: EP-A-1604666, and refused the grant

The learned counsel for the appellant submitted that the aim of the invention is intended to be a Dosage Form in a specific patient population who are

not only suffering from pain but also experiencing side effects due to opioid pain therapy (particularly constipation) and also adverse events

(particularly diarrhea) due to active agent naloxone in the dosage form. This invention lies in the dosage form capable of providing pain relief as well

as an optimal balance between side effects and adverse events as described above.

2. The learned counsel referred to the complete specification which refers to the embodiment examples and the optimization of naloxone and

oxycodone ratio in patients suffering pain. The learned counsel also refer to the estimated improving by using oxycodone naloxone ratio versus

naloxone placebo groups

The estimates indicate that bowel function improvement increases as oxycodone/ naloxone ratio decreases, with the estimated improvement at 2:1

approximately 50% higher than at 4:1 (p 3. The learned counsel also refers to the complete specification:

Opioid analgesics are considered to be strong agonists if they bind with high affinity to opioid receptors and induce a strong inhibition of pain reception.

Substances that also bind with high affinity to opioid receptors, but that do not cause a reduction of pain reception and which thereby counteract the

opioid agonists, are designated as antagonists. Depending on the binding behavior and the induced activity, opioids can be classified as pure agonists,

mixed agonists/antagonists and pure antagonists. Pure antagonists comprise, for example, naltrexone, naloxone, nalmefene, nalorphine, nalbuphine,

naloxocazinen, methylnaltrexone, ketylcyclazocine, norbinaltorphimine, naltrindol, 6-B-naltrexone (Forth W.; Henschler, D.; Rummel W.; Starke, K.:

Allgemeine und Spezielle Pharmakologic und Toxikologie, 7, Auflage, 1996, Spektrum Akademischer Verlag, Heidelberg Berlin Oxford).

Other attempts aim at minimizing the addictive and habituation forming potential of opioid analgesics, as well as their other side effects by the

administration of antagonists which counteract the opioid analgesic. Such antagonists might be naltrexone or naloxone.

4. The learned counsel submitted that an object of the present invention is to provide an oxycodone Naloxone dosage form which provides a fast

analgesic effect and, at the same time, is suitable in chronic maintenance therapy. There were originally 26 claims, claim 1 being the independent claim

and the others being dependent claims. Claim 1 originally read as follows:

A dosage form comprising oxycodone and/or a pharmaceutically acceptable salt

thereof and naloxone and/or a pharmaceutically acceptable salt

thereof, which provides a tmax for oxycodone or a pharmaceutically acceptable salt at about 1 to about 17 hours, at about 2 to about 15 hours, at

about 3 to about 8 hours or at about 4 to about 5 hours after single dose administration to healthy human subjects.

5. The learned counsel made it clear that the ratio between oxycodone and naloxone must be maintained at 2:1. According to the learned counsel, the

Controller erred in rejecting the claims has being un-clear. According to her, the application clearly shows the dosage form and how the side effect

improved in patients. Therefore it was clear for which patient group the dosage form was intended. The learned counsel also submitted that the AUCt,

and Cmax had been defined in the application and in any event a skilled person in this art would be aware of how to adopt the formulation and

guidance for the skilled person in this respect.

6. The learned counsel then submitted that their letter dated 17.08.2009 and petitioner had also been filed to condone the delay. However, by mistake

it was typed as petition under rule 138 instead of 137.

7. The learned counsel submitted that the prior art '504 shows that it was sustained release of one pharma active compound whereas the invention

optimizes treatment of the problem which is both constipation and diarrhea. The claims of 504 only speak of sustain release of one compound which is

pharmacologically action. The other prior art '802 while it talks of pharmacological combination of Oxycodone and Naloxone does not lead to the

invention because it combine Naloxone in a very low proportion. The next prior art '060 (PCT 22), the learned counsel submitted that it was addressed

to euphoric effect of opioid but there was nothing here to teach towards the invention.

8. The learned counsel referred to European Patient '666 which was for patients with Chronic Obstructive Pulmonary Disease (COPD) there is no

recognition of the problem which the invention addressed. She also referred to the experts statement given by Michael Hopp who is one of the

inventor. This affidavit refers to the side effects associated with opioid agonists, the problems faced by chronic pain patients and the advantage of

using 2:1 ratio over the ratio of 1.5:1 and that a dosage form comprising oxycodone and naloxone in a 2:1 ratio is particularly suited for the treatment of

patients suffering not only from pain but which would also suffer from opioid induced side effects and particularly diarrhea as naloxone induced

adverse event. The learned counsel therefore submitted that the Controller had erred in rejecting the patent.

9. It is clear from the submissions made by the counsel as well as grounds that the aim of the present invention is in providing a dosage form which

relieves the pain and balances the side effects associated with opioid therapy, the analgesic and adverse events associated with opioid antagonist and

that the ratio of 2:1 of Oxycodone to Naloxone is surprisingly superior over a ratio of 1.5:1. According to the appellant the distinguishing features of

the invention lies in the effect seen in the new patient group and the invention solved the technical problem by providing the dosage form wherein

Oxycodone and Naloxone are present in a ratio 2:1 by weight and that D1 does not hint that 2:1 is the most suitable and superior ratio.

10. They have also filed M.P. No. 12/2011 for early hearing and M.P. No. 13/2011 for amendment of the claims, in accordance with the claims

accepted in European Patient and Russia. Prior art '504 is an invention that belongs to the appellant. It is a matrix for sustained, invariant and

independent release of active compounds. At page 5 of this prior art, there is reference to the side effect that may go along with the Oxycodone and

the side effects are, amongst others, breath depression and obstipation. Obstipation is severe constipation. This prior art says that ""if patents seeking

pain release are treated with preparations comprising an opioid, analgesic, simultaneous treatment with preparations comprising antagonists such as

naltrexone or naloxone may be desirable in order to counteract the aforementioned side effects"". This prior art states that on that date sustained

release formulation were not available. Many attempts had been made to eliminate the habit forming potential of opioid, analgesic and their other side

effects.

11. One of the objects of this invention was to provide pharmaceutical preparations to ensure sustained release and stability over a long period.

12. Page 13 of the prior art deals with the preparation of a formulation containing 12 mg oxycodone and 6 mg naloxone. According to this invention,

the increase of naloxone from 4 mg to 6 mg does not change the release behaviour.

13. Page 26 of this prior art, says that especially preferred antagonists is naloxone and formulations with a combination of oxycodone as against and

naloxone as antagonist are particularly preferred. The agonist is preferably in excess compared to the antagonist. Amongst the preferred weight ratio

ranges between 15:1 and 1:1, we find 2:1. It also says that whenever oxycodone and naloxone is mentioned it comprises pharmaceutical acceptable

and equally acting derivatives, salts and the like.

14. At page 33 of the prior art, there is again reference to a formulation comprising oxycodone and naloxone. Example 1 specifically refers to

oxycodone and nalaxone. Whether the ration is 2:1. The fact that this invention claims a pharmaceutical formulation comprising atleast one active

compound does not mean that it teaches a way from the invention.

15. Claim 11 of this prior art speaks of pharmaceutical preparation, characterized in that it comprises opioid analgesics as the pharmaceutically active

compounds, preferably morphine, oxycodone, hydromorphone, proposyphene, nicomorphine, dihydrocodeine, diamorphine, papaveretum, codeine,

ethylmorphine, phenylpiperidine and/or derivatives thereof, methadone, destropropoxyphene, buprenorphine, pentazocin, tilidine, tramadol and

hydrocodone and/or opioid naloxonazinene, methylnaltrexone, ketylcyclazocine, norbinaltorphimine, naltrindol, 6-b-naloxol and/or 6-b-naltrexol.

16. Claim 13 of this prior art, speaks of pharmaceutical formulation characterized in that the formulation comprises atleast two active compounds

which are oxycodone and naloxone.

17. Claim 14 of '504 is for a pharmaceutical formulation characterized in that it comprises oxycodone and naloxone in a weight ratio ranging from

maximal 25:1, preferably maximal 20:1, 15:1 and more preferably from 5:1, 4:1, 3:1, 2:1 and 1:1.

18. Next we will take up '802 prior art which is owned by the appellant and it (discloses in certain embodiments ""a pharmaceutical composition

comprising from 10 to 40 mg of oxycodone or a pharmaceutically acceptable salt thereof and 0.65 to 0.90 mg naloxone or a pharmaceutically

acceptable salt thereof"".

19. The objects and summary of the invention shows that it is directed to a pharmaceutical composition comprising from 10-40 mg of oxycodone and

.65 to .90 naloxone. In certain embodiments of the invention, the dosage form

comprises a matrix comprising the oxycodone hydrochloride and the

naloxone hydrochloride interdispersed in a sustained release excipient. It is evident from the above that there is no novelty or inventive step. The

combination of Oxycodone-Naloxone to treat patients was known and this formulation is the ratio 2:1 is also known.

20. We however, differ from the Controller that S.8 disclosure was not made in time. It is seen that they have prayed for condonation of delay. That is

accepted.

21. It is curious why the complete specification do not mention either of the prior arts which belong to the appellant. There is a duty of disclosure of

materials affecting patentability, though it is not explicitly stated of the law. Particularly in respect of application origination under PCT where in other

jurisdiction the applicant is liable to include prior art if not included at the time of filing of the applicant. In The US PTO it is mandatory to disclose

prior arts. Here we reiterate again what we said in OA/2/2010/PT/CH in Para 40.

40. Considering the fact that by a grant of patent, the applicant gets an exclusive monopoly in his invention, a full and fair disclosure of what is known

to him is perhaps only to be expected. The patent applicant cannot leave it to the Controller and to the streaming download of knowledge from the

computer at the Controller's finger tip. The applicant ought to have referred to the prior art D1 in the specifications since the common specification for

D1 and the invention are almost identical. We are sure in the near future, there will be better drafting standards.

We confirm the finding of the Controller that there is no new invention or inventive step. Therefore the appeal is dismissed. Miscellaneous Petition

Nos. 12 & 13/2011 are closed.

