Neutral Citation Number: [2024] EWCA Civ 128

Case No: CA-2023-001357

IN THE COURT OF APPEAL (CIVIL DIVISION)
ON APPEAL FROM THE HIGH COURT OF JUSTICE, BUSINESS AND PROPERTY COURTS OF ENGLAND AND WALES, INTELLECTUAL PROPERTY LIST (ChD)
Recorder Douglas Campbell KC
[2023] EWHC 1471 (Ch)

Royal Courts of Justice
Strand, London, WC2A 2LL

Date: 15/02/2024

Before :

LORD JUSTICE LEWISON
LORD JUSTICE MOYLAN
and
LORD JUSTICE BIRSS

- -

Between :

Newron Pharmaceuticals S.p.A.	**Appellant**
- and -	
The Comptroller General of Patents, Trademarks and Designs	**Respondent**

- -
- -

Richard Davis KC (instructed by **Mathys & Squire LLP**) for the **Appellant**
Dr Stuart Baran (instructed by **Governement Legal Department**) for the **Respondent**

Hearing dates: 24 January 2024

- -

Approved Judgment

This judgment was handed down remotely at 10.30am on [date] by circulation to the parties or their representatives by e-mail and by release to the National Archives.

.....

Lord Justice Birss:

1. The question in this appeal is about the meaning of the term "product" in Article 3(b) of Regulation (EC) No. 469/2009 concerning supplementary protection certificates for medicinal products. The question arises in the context of a treatment for Parkinson's disease using an agent called safinamide (brand name Xadago). Xadago has been authorised for the treatment of that illness as an add-on therapy to levodopa (L-dopa) given alone or in combination with other Parkinson's disease medicines.

2. Supplementary protection certificates (SPCs) are a form of patent term extension to compensate for lost time caused by the marketing authorisation regime applicable to pharmaceutical products and such like. The normal 20 year patent term starts when the patent is applied for, once the invention of the new drug as a treatment for a given disease has been made. However the law prevents the marketing of such a product as a medicine without authorisation, and the authorisation is only given on proof to the appropriate authority that the product is a safe and effective medicine for the disease concerned. That proof is only possible after extensive, costly and uncertain clinical trials have been completed to establish safety and efficacy. That takes time, and the result is that the patentee cannot begin to recoup its investment in research and development, by marketing the pharmaceutical, for some years later than would have been possible absent the marketing authorisation regime. Thus the SPC system will extend the relevant term for up to five years provided the various criteria are satisfied (see Recitals [3] to [8] of the SPC Regulation and also *Draco's SPC Application* [1996] RPC 417 at 436).

3. To apply the criteria one needs to examine two relevant documents – the patent and the marketing authorisation. Put briefly, a critical requirement for an SPC to be granted is that the patent and the marketing authorisation must match. In the language of the SPC Regulation the product authorised to be placed on the market as a medicinal product by the relevant marketing authorisation must be the product protected by the relevant patent. In this case the problem for the appellant is that the Hearing Officer acting for the Comptroller, upheld on appeal to the High Court, concluded that the product authorised by the marketing authorisation was not the same as the product protected by the patent.

4. The patent is EP (UK) 1 613 296 entitled "Methods and Treatment of Parkinson's Disease" filed on 8 April 2004. The patent will expire on 7 April 2024. Claim 1 of the patent is in this form:

> "1. The use of a first agent selected from safinamide from 0.5 to 1, 2, 3, 4 or 5 mg/kg/day in combination with levodopa/PDI, for the preparation of a medicament as a combined product for simultaneous, separated or sequential use for the treatment of Parkinson's disease."

5. As the judges below explained, the expression PDI in this claim is an abbreviation for Peripheral Decarboxylase Inhibitor. The role of the PDI is to inhibit the breakdown of levodopa while travelling through the bloodstream of the body to the brain. Once the levodopa crosses the blood-brain barrier, which the PDI cannot, the levodopa exerts its therapeutic effect. The use of levodopa with a PDI was already a known treatment for Parkinson's disease.

6. This case has proceeded on the undisputed basis that claim 1 relates to a combination of three active ingredients: safinamide, levodopa and PDI; and that within the language of the SPC regime, it is this combination which is the "product" protected by the relevant patent (see art 3(a) of the SPC Regulation below).

7. The relevant marketing authorisation is a Commission decision dated 24 February 2015 under Regulation (EC) 726/2004. The issue is about what it authorises.

8. The Hearing Officer Dr Cullen held that the marketing authorisation was not an authorisation for the combination mentioned above. The reason was a simple finding that the marketing authorisation was in fact for the active ingredient safinamide alone, and not a combination. This was in paragraphs [43]-[54] of Hearing Officer's decision. The main reasons why this was so were because the Commission decision itself refers only to "Xadago-safinamide" and does not mention levodopa or PDI, and when one turns to the Summary of Product Characteristics (SmPC) forming Annex 1 to the marketing authorisation decision, the medicinal product is identified simply as Xadago (safinamide), in the form of a 50mg tablet, and not a combination.

9. It is true that the "Therapeutic indications" section (part 4.1) of the SmPC makes clear that Xadago is indicated for "the treatment of *[...]* Parkinson's disease (PD) as add-on therapy to a stable dose of Levodopa (L-dopa) alone or in combination with other PD medicinal products *[...]*", and there are further similar references deeper in the SmPC. However the Hearing Officer held that this material does not alter what product is here authorised to be placed on the market as a medicinal product. At most it describes how the medicinal product is to be used, but such features are not part of the definition of product. The marketing authorisation in this case authorises the product safinamide to be placed on the market as the medicinal product Xadago and that is all.

10. On appeal Recorder Douglas Campbell KC upheld that conclusion at [31] – [50]. On this appeal Newron contends that this was or involved errors of law. In particular the question of law revolves around the distinction between what a product is and how it is to be used. That is the first ground of appeal.

11. The Hearing Officer also did not accept that the marketing authorisation related to a combination in which PDI was an element, even if (which was not accepted) it did relate to safinamide in combination with levodopa. This was dealt with in paragraphs [55]-[59] of the decision. This was also upheld on appeal ([51]-[54]). That is the second ground of appeal. It only arises if the first ground succeeds.

First ground

12. The SPC Regulation is an EU instrument but is now retained EU law, and has not materially changed since Brexit.

13. The relevant provisions of the Regulation are parts of Articles 1 and 3, as follows:

"Article 1 Definitions

For the purposes of this Regulation, the following definitions shall apply:

> (a) 'medicinal product' means any substance or combination of substances presented for treating or preventing disease in human beings or animals and any substance or combination of substances which may be administered to human beings or animals with a view to making a medical diagnosis or to restoring, correcting or modifying physiological functions in humans or in animals;
>
> (b) 'product' means the active ingredient or combination of active ingredients of a medicinal product;
>
> *[…]*
>
> Article 3 Conditions for obtaining a certificate
>
> A certificate shall be granted if, in the Member State in which the application referred to in Article 7 is submitted and at the date of that application:
>
> (a) the product is protected by a basic patent in force;
>
> (b) a valid authorisation to place the product on the market as a medicinal product has been granted in accordance with Directive 2001/83/EC or Directive 2001/82/EC, as appropriate;
>
> (c) the product has not already been the subject of a certificate;
>
> (d) the authorisation referred to in point (b) is the first authorisation to place the product on the market as a medicinal product.
>
> *[…]*

14. Although the question is what the product is, to understand how the scheme works it helps to start from the medicinal product. That is defined in Art 1(a) of the SPC Regulation essentially as any substance or combination of substances presented for treating a disease. It is no accident that the definition is the same as the one used for medicinal product in the relevant marketing authorisation legislation (such as Directive 2001/83/EC at Art 1 (2), and Regulation (EC) 726/2004 to which it refers at Art 2). In other words, naturally enough, the scheme of the SPC Regulation starts with a concept taken from the marketing authorisation legislation.

15. Now one can see what a "product" is. Art 1(b) defines it as the active ingredient or combination of active ingredients of a medicinal product. Following from this one can apply Art 3, noting that the concept which links the four criteria in that article together is the product. At Art 3(a) the product must be protected by the patent, at 3(b) there must be a marketing authorisation to place the product on the market as a medicinal product, and so on in Art 3(c) and 3(d).

16. It is manifest that the meaning of product cannot be different in these various limbs of Art 3, and before us Newron did not contend otherwise.

17. Counsel for the Comptroller also drew attention to the Explanatory Memorandum COM (90) 101 final, 1990 OJ C 114/10 which was promulgated by the European Commission. It is clear from this, and from the recitals to the SPC Regulation itself, that the overall scheme seeks to strike a balance between various interests at stake, including the interests of those carrying out pharmaceutical research, public health and generic manufacturers. However as Counsel for the Comptroller also submitted, the balance is itself struck by the terms of the SPC Regulation. It is not a balancing exercise which courts are invited to undertake on a case by case basis.

18. The Explanatory Memorandum at [16] shows that the scheme is intended to be a simple transparent system which can easily be applied by the patent offices concerned. That point has a bearing on a detail in argument (below) about how involved the consideration of the marketing authorisation ought to be.

19. The relevant EU case law can be divided into three parts.

20. The early cases are C-31/03 *Pharmacia Italia SpA* [2004] ECR I-10001; C-431/04 *Massachusetts Institute of Technology* [2006] ECR I-4089 and C-202/05 *Yissum Research and Development Company of the Hebrew University of Jerusalem v. Comptroller-General of Patents* [2007] ECR I-2839. Collectively these stand for the proposition that what a product amounts to is the active ingredient itself and it does not involve taking into account any formulation of the active ingredient into drug (such as excipients, physical form or the like) or the intended use for it. So in *Yissum* at [17] the CJEU held that the concept of product referred to in Article 1(b) "must be interpreted strictly to mean 'active substance' or 'active ingredient'". The strictness there refers to the exclusion of other aspects such as formulation and use.

21. Next is *Neurim Pharmaceuticals v Comptroller* C-130/11 [2012] EPC 23. Here the CJEU (and Advocate General Trstenjak) followed a persuasive judgment of the Court of Appeal in the referring case by Jacob LJ giving the judgment of the court with Patten and Smith LJJ ([2011] EWCA Civ 228). That judgment proposed that contrary to the early CJEU cases, the use to which a product is put *should* be taken into account, in order to achieve the result of encouraging research into new uses for old ingredients. So in *Neurim* the CJEU held that the use could play a role in the analysis. Nevertheless a notable aspect of the CJEU's judgment in *Neurim* was that while it appeared to reverse the three early cases referred to above, it did not refer to them or explain the change. Later in this jurisdiction in *Abraxis v Comptroller* [2017] EWHC 14 (Pat) Arnold J at [32] – [38] noted these and other difficulties with the CJEU's judgment in *Neurim*.

22. Finally in July 2020 what might be called orthodoxy was restored in *Santen* C-673/18. The CJEU there held that the definition of product in the SPC Regulation did not include the therapeutic application for which it might be used (see [43]) and went out of its way to expressly contradict (at [53]) what had been said about this in *Neurim*. At [44] of *Santen* the court said this:

> "44. Under Article 4 of *[the SPC Regulation]*, the protection conferred on the product by the SPC, although it extends only to the product covered by the MA, covers, on the other hand, any use of that product as a medicinal product which was authorised before the expiry of the SPC. It follows that the term

> 'product' within the meaning of Regulation 469/2009 *is not dependent on the manner in which that product is used* and that the intended use of the medicinal product does not constitute a decisive factor for the grant of an SPC (see, to that effect, judgment of 19 October 2004, *Pharmacia Italia*, C-31/03, EU:C:2004:641, paragraphs 19 and 20)."
>
> [*emphasis added*]

23. That deals with the main authorities relevant to this case but there are two other decisions to refer to. First in 2010 Lewison J in the Patents Court in *Yeda v Comptroller* [2010] RPC 29 dismissed an appeal from the decision of Dr Cullen as the Comptroller's Hearing Officer refusing to grant an SPC in circumstances similar to the present case. The relevant marketing authorisation in that case was for a medicinal product called Erbitux, the active ingredient of which was a product called cetuximab, for treating certain cancers. The SmPC did explain how the Erbitux was to be used, and that included a statement that Erbitux in combination with another drug called irinotecan was indicated for the treatment of certain cancers. The patent claimed the combination of cetuximab and an anti-neoplastic agent (which could be irinotecan).

24. The patentee applied for an SPC, based on the patent and marketing authorisation. In fact there were two parallel applications whereby the patentee ran alternative cases. In the 037 application the patentee contended that the relevant product was the combination of cetuximab and irinotecan whereas in the 038 application the product was defined as cetuximab alone. Both failed. The former (037) failed because although the patent could be said to protect the product defined that way as a combination, the marketing authorisation was not an authorisation to place that combination product on the market as a medicinal product. The latter (038) failed because the patent did not protect cetuximab alone, it claimed a combination. The important aspect for present purposes is the 037 application.

25. The Hearing Officer held (at [40]) that the relevant approach in law was as follows:

> "*[…]* I have to concern myself with determining what exactly is the medicinal product that has been approved and not just with its use or uses. Furthermore, such a focus on what the product is, rather than what it does, is consistent with the fact that what it does can change in the life of the MA but the product itself does not. *[…]*"

26. This was upheld by Lewison J who said at [26]:

> *[…]* But as the case law shows, how a medicinal product is used does not form part of the identification of the product itself. In my judgment the brief references to irinotecan in explaining how cetuximab is used are wholly insufficient to amount to a marketing authorisation of a product consisting of both cetuximab and irinotecan. In short, I agree with the hearing officer for the reasons that he gave."

27. I respectfully agree with this. Stated in 2010 it anticipated, and is now entirely in line with the CJEU's reasoning in *Santen* at [44] to which I drew attention above.

28. The final case to mention is the CJEU's decision and the Opinion of Advocate General Trstenjak in *Medeva v Comptroller* Case C-322/10 [2012] RPC 25. That case was decided in 2011, the year before *Neurim* in the CJEU. *Medeva* was concerned with vaccine compositions and in one respect (question 6) concerned a converse situation to the present case. There the patent protected a single ingredient or combination while the marketing authorisation authorised a product involving a combination including the patented ingredient or combination, but also requiring at least one further active ingredient. So if the patent protected active ingredients A+B the marketing authorisation authorised active ingredients A+B+C.

29. Counsel for Newron focussed on the opinion of the AG and submitted that the view expressed there (particularly at [89]) was that a broad or teleological approach to the definition of product and to the effect of Art 3(b) should be taken in order to achieve the purposes of the SPC Regulation in the context of vaccines and the need to encourage multivalent vaccines. Therefore the SPC should not be precluded in that case. The CJEU itself did reach the same conclusion on the question referred. Its reasoning is inevitably more compressed but it is right to note that although the term "teleological" is not used by the court, the reasoning is essentially the same as that of the AG. The CJEU adopted an outcome driven approach determined by a view about what the purpose of the scheme was and that a result which did not lead to an SPC in that case would be undesirable and wrong.

30. While Newron's submission is understandable, in my judgment *Medeva* does not alter the law as I have found it to be from looking at the run of CJEU authority up to *Santen*. It was a broader, outcome driven teleological approach in *Neurim* itself which led to the difficulty in that case making it inconsistent with a run of previous authority. *Santen* concludes that the right approach to interpreting the SPC Regulation in the present context is a strict one when one is examining what counts as the product. Necessarily the decision also shows that while the purpose of the SPC Regulation is in turn to support the purpose of the patent system as a scheme for incentivising investment in research, nevertheless not all kinds of inventions, deserving of patents though they all may be, will be able to obtain an SPC.

31. Finally counsel for Newron submitted, accurately, that none of the earlier CJEU cases had considered facts like the present case. So when the idea is expressed that the definition of product is not dependent on the manner in which that product is used, what the cases were concerned with as the "manner of use" was either applications of the active ingredient (i.e. treating a disease) such as in *Neurim* or extra inactive compounds of some kind alongside the active ingredient such as in *MIT*. A combination of a first active ingredient with another active ingredient, such as the levodopa and/or PDI in this case, had never been addressed before in this way or characterised as a manner in which the first active ingredient was used.

32. That submission is true but it does not help. The question in the end under Art 3(b) is whether, assuming the product in question is safinamide in combination with levodopa and PDI, the marketing authorisation in the present case is an authorisation to place that on the market as a medicinal product. It is clearly possible to conceive of a marketing authorisation of that sort, with all three of those ingredients named in

combination in the decision and the SmPC as comprising the medicinal product. However if the court and the Hearing Officer below were right to identify that the role played by Levodopa and PDI in the present marketing authorisation was at best an aspect of the manner in which the product safinamide was to be used, then their decisions to refuse the SPC and to uphold that refusal, were a correct application of the law.

33. Turning to the facts of this case and applying the law above, in my judgment the Hearing Officer and the judge were right in their conclusion that the product which this marketing authorisation authorises to be placed on the market as a medicinal product is safinamide. It is not a combination.

34. I am quite sure both the Hearing Officer and the judge interpreted the marketing authorisation in this case correctly. The Commission decision itself only mentions Xadago-safinamide and first two sections of the SmPC which name the medicinal product and state its composition, identify simply Xadago as the name and the only active ingredient identified is safinamide. It is true that the only therapeutic indication mentioned in the relevant section of the SmPC is add-on therapy with Levodopa alone or in combination, but this mention of Levodopa is clearly an aspect of how the product safinamide is to be used. It is not an active ingredient in the medicinal product authorised by this marketing authorisation.

35. I agree with counsel for the Comptroller that the fact the SPC scheme is meant to be relatively simple to administer by a patent office has a bearing here, in that it ought not require minute analysis of the lengthy detailed annex to a marketing authorisation to answer the relevant question. The fact there are further references to Levodopa and (a few) to PDIs in the detailed parts, along with references to the clinical trials involving both, is not relevant to the fairly simple question what is the active ingredient in the medicinal product authorised by a given marketing authorisation. In the appeal the appellant sought permission to include new expert evidence examining the marketing authorisation. In the High Court the appellant had also sought permission on that appeal to admit similar expert evidence in a longer form. The judge below refused and there was no appeal. Surprisingly the appellant then made a fresh application to this court to admit a slightly shorter version of this same evidence. We refused that application at the hearing not least because it was plainly material which could and should have been deployed at the first instance before the Hearing Officer. Nevertheless it is also worth making the point that with the law as explained above, evidence of that kind ought to be unnecessary.

36. A point which emerged in argument before this court and which I believe puts the matter beyond doubt, is to focus on what exactly it is that the holder (Newron) is authorised to do as a result of the marketing authorisation in question. The answer here is that this marketing authorisation authorises Newron to market Xadago (safinamide). That is all. There is no dispute that this marketing authorisation does not authorise Newron to put on the market any other active ingredient such as Levodopa (nor other PDIs). The evidence does not address whether Newron sells Levodopa, it does not matter. However if Newron was putting Levodopa on the market at the moment there would need to be a further marketing authorisation for that.

37. I would therefore dismiss this appeal on the first ground.

38. On that basis there is no need to examine the second ground, which cannot help if the first ground fails. I will only add this. The premise on which the second ground arises has to be that the first ground had succeeded, in other words that as a result of the references in this marketing authorisation to the therapeutic indication being add-on therapy with Levodopa, the product authorised by the marketing authorisation should be seen as a combination of at least safinamide and Levodopa. As I have explained I disagree with that, but if that is the conclusion it can only be because one is required to examine and put weight on what ways of using safinamide are contemplated by the marketing authorisation. If a PDI is an active ingredient at all, which I have some doubt about but was not in dispute on this appeal, and if the marketing authorisation does contemplate using safinamide in add-on therapy with both Levodopa and PDI, which it plainly does albeit you have to read a lot of detail to find it and albeit other ways of using it, without PDIs, are contemplated too, then I am not so sure about the second ground. But it is not necessary to express a concluded view about that.

39. I would dismiss the appeal.

Lord Justice Moylan:

40. I agree.

Lord Justice Lewison:

41. I also agree.