Decision in the matter of SPC application 2015/043.

Applicant: Newron Pharmaceuticals S.p.A.

Hearing Date 17 January 2024

Hearing Officer: Dr Fergal Brady

DECISION

Introduction

1. This decision concerns the Request for a Supplementary Protection Certificate numbered 2015/043 (the 'Request'), filed by Newron Pharmaceuticals S.p.A (the 'applicant') under Regulation (EC) 469/2009 (the 'SPC regulation').

2. The Request was filed on 21 July 2015, relying on the basic patent EP 1613296 B1, a European patent filed on 08 April 2004, which upon grant on 01 July 2009 became a valid granted patent in Ireland. This patent is titled 'Methods for Treatment of Parkinson's Disease'.

3. The Request further relied on a European Market Authorisation no. EU/1/14/984/001-010, for the product Xadago®-Safinamide made under Regulation (EC) 726/2004 on 24 February 2015, and notified on 26 February, and which is valid in Ireland.

4. The product, as identified in the Request, is *'Safinamide for use in combination with levodopa/PDI, and optionally with other PD products, for the treatment of Parkinson's Disease.'* The applicant declared in the request that the product is protected under claims 1-8 of the basic patent.

5. On 16 July 2017, the examiner issued an official letter indicating a deficiency in the Request, in that though the Request is directed towards safinamide in combination with other active substances, the Market Authorisation only identifies safinamide as the active substance in the product. Thus, the examiner deemed that the Request was defective, as it did not meet the requirements of Art 3(b) of the SPC regulation. This argument has formed the main substance of the objection made to the grant of the Request.

6. The examiner also drew the applicant's attention to their view that were the applicant to amend the request such that the product constituted safinamide alone, it would not be supported by the basic patent and would not instead meet the requirements of Art 3(a) of the SPC regulation. It is noted that, while the applicant has presented argument in this matter, they have not at any point formally requested to change the product identity to safinamide alone, so this argument is not directly relevant in the present circumstances. Indeed, it was agreed by the applicant's agent at the Hearing that the issue to be resolved rests solely on whether the Request meets the requirements of Art 3(b). I note that the applicant did indicate

a willingness to make such a change in paragraph 44 of the pre-Hearing submission, although they rejected this idea in the Hearing itself.

7. The fundamental issue to be determined is therefore whether, as per Art. 3(b), the product, that is 'Safinamide for use in combination with levodopa/PDI' is covered by the market authorisation:

> *a valid authorisation to place the product on the market as a medicinal product has been granted in accordance with Directive 2001/83/EC*.

Product, of course, as per Article 1(b) means

> *the active ingredient or combination of active ingredients of a medicinal product*.

The Product

8. The applicant identifies the product in the following way: *Safinamide for use in combination with levodopa/PDI, and optionally with other PD products, for the treatment of Parkinson's Disease.'* I construe this to mean a combination of (at least) safinamide and levodopa/PDI. That is to say, the safinamide must be used in combination with the levodopa/PDI.

9. The applicant does make some argument that the product is safinamide alone, but I do not accept this argument. If safinamide is for use in combination, then the Request does indeed concern a combination. The applicant has been free throughout proceedings to alter the product identity, to make explicit a desire for safinamide alone, but has not chosen at any point to do so, retaining the present wording for the product identity throughout the entire prosecution of the Request.

10. More significantly, in paragraph 15 of the pre-Hearing submission, the applicant, having already noted that "the present Application is concerned with a combined therapy" (see paragraph 14 of the pre-Hearing submission) states that:

> *The product in question is a combination of active ingredients and Article 1(b) of the Regulation is explicit: a product may be a combination of active ingredients.* (underlining is the applicant's own)

Therefore, I am correct in interpreting the identified product as a combination, since that is the expressed and emphatic view of the applicant. That combination is necessarily one of safinamide and levodopa/PDI.

The Basic Patent

11. The patent comprises 8 claims. Claim 1 is as follows:

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.

12. This claim clearly establishes that safinamide is used in combination with levodopa/PDI. Levodopa is used to treat Parkinson's Disease (PD). As set out in paragraph 2 of the patent, this disease is indicated by the specific degeneration of dopamine-containing cells in the substantia nigra of the midbrain. This in turn leads to a deficiency of dopamine in the striatum, which leads to the debilitating symptoms experienced by those suffering from this condition. Levodopa is considered the single most effective drug for treatment of patients, but after 5-7 years of treatment, there is a deterioration in the patient's response to this treatment, referred to as Late Motor Fluctuations (LMF), which can seriously adversely affect the patient's health. While levodopa may itself facilitate the onset of LMF, substitution with other dopamine agonists does not yield the same level of symptom relief.

13. The term levodopa/PDI should also be explained. Levodopa treats PD by boosting dopamine levels in the striatum. To do this, it must migrate from the point of physical administration to the brain, but it is vulnerable to metabolism while on that journey. For this reason, it is generally administered with a co-drug, a peripheral decarboxylase inhibitor (PDI) which prevents the peripheral metabolism (that is, its metabolism by carboxylase enzymes before reaching the target area) of the levodopa. So, the term levodopa/PDI is to be understood as a co-administration of two medicaments, levodopa AND the inhibitor, and not a choice between levodopa and the PDI. The safinamide is therefore to be understood for use in combination with pairing of levodopa and a PDI. Indeed, claim 2, which is dependent on claim 1, clarifies that levodopa/PDI is a combination in itself, as it sets out various combinations from which the levodopa/PDI pairing can be selected. This claim is followed by three more claims (3-5) dependent ultimately on claim 1.

14. Returning to claim 1 itself, the applicant argues (paragraphs 6-7 of the pre-hearing submission) that this, being a kit-of-parts, can be construed as a claim for safinamide alone. I cannot agree with this. The claim ties safinamide and levodopa/PDI as a combination twice, firstly stating that the safinamide is in combination with levodopa/PDI, and secondly stating that the medicament is a combined product. This is not surprising, given that the patent indicates, and the applicant concedes, that safinamide is not of medicinal value in the absence of levodopa/PDI. The use of kit-of-parts wordings are not a magic bullet, in that there must be functional unity between the parts of the kit in order to give patency to the claimed invention. Safinamide only has value as a medicament in this context because of its use in combination with levodopa/PDI, and this must be kept in mind when interpreting this claim.

15. Claim 6 sets out a kit for treating PD, as follows:

6. A kit for treating a patient having Parkinson's Disease, comprising a therapeutically effective dose of a first composition comprising safinamide from 0.5 to 1, 2, 3, 4 or 5

mg/kg/day and a second composition comprising levodopa/PDI, either in the same or separate packaging, and instructions for its use.

16. As such, this claim sets out the use of safinamide in combination with levodopa/PDI, in the form of a kit, which the applicant also identifies as a kit-of-parts. Kit-of-parts claims rely, as already noted above, on a functional unity between the otherwise separate parts of the kit. Whether, as the applicant has argued (see paragraphs 23-31 of their pre-Hearing submission), the safinamide and levodopa/DPI are packaged separately is not to me relevant, because the kit, taken as a whole, must comprise both items to give it patency. It is not, therefore, a vehicle for the single and exclusive medicinal use of safinamide, but a combination.

17. Indeed, if it were reasonable to suppose that this claim allowed the separate and distinct use of safinamide without regard to the levodopa/PDI element, as the applicant argues, it is equally the case that the claim would similarly allow the separate and distinct use of levodopa/PDI, which is clearly neither novel or inventive. Further, the applicant has allowed, both in oral and written testimony in the hearing and by reference to the basic patent, that safinamide alone is of no real medicinal value. For this reason, I construe this claim to be a combination claim, since it is necessary that the safinamide and the levodopa/PDI are both available for use in some form of combination.

18. Claim 7 sets out a pharmaceutical composition, as follows:

7. A pharmaceutical composition comprising effective amounts of safinamide from 0.5 to 1, 2, 3, 4 or 5 mg/kg/day and of levodopa/PDI.

This claim, which has one dependent claim, clearly sets out a combination of safinamide and levodopa/PDI.

19. All the claims therefore concern a combination of safinamide and levodopa/PDI, and are therefore consistent with the combination product identified in the request.

The Marketing Authorisation

20. The authorisation presented in conjunction with the present request is a European authorisation for the product 'Xadago[®] – Safinamide', the implementing decision for which was issued by the European Commission on 24 February 2015.

21. Annex 1 thereto identifies, under Heading 1, Xadago® as the medicinal product, in the form of 50 mg film-coated tablets. Under Heading 2, it states that these tablets contain safinamide methansulfonate equivalent to 50mg free safinamide, as the sole active ingredient.

22. This medication is indicated under Heading 4.1 as an add-on therapy for those with idiopathic Parkinson's Disease, who are receiving a stable dose of levodopa, either on its own or with other medications for their condition. While it makes clear that the administration of safinamide occurs in conjunction with an existing regimen of levodopa, the authorisation does

not authorise this co-administration, but merely the administration of safinamide itself. To be absolutely clear, the present marketing authorisation does not in any way authorise the administration of levodopa, but solely safinamide.

The Issue

23. The examiner, Dr Cassidy, raised the objection that, because the basic patent is directed to a combination, (i.e. to safinamide in combination with Levodopa/PDI) while the marketing authorisation is directed solely to safinamide, the request does not meet with the requirements of Article 3(b) of Regulation EC 469/2009, since they do not cover the same product.

24. Dr Cassidy also noted that to alter the request to direct exclusively to safinamide would not solve the issue, since safinamide alone is not protected by the basic patent, as required under Art. 3(a) of the Regulation.

25. In the Hearing the applicant accepted that the question rests solely on whether the Request is compliant with Art. 3(b). They set out a number of arguments as to why grant of the Request was justified. The main one rests on the nature of add-on therapies. In this argument, the applicant asserts that since the patient receiving the safinamide is already receiving Levodopa, the safinamide administered to said patient is by definition in combination with Levodopa. That is to say, it is clear that the administration of safinamide is an add-on therapy. Indeed, the applicant noted in the hearing (by reference to paragraph 46 of the basic patent) that safinamide administered alone is of virtually no therapeutic value. While what the applicant say is factually correct, it constitutes, to my mind, an attempt to define the product in terms of intended use rather than the active ingredient per se.

26. The applicant argues (in paragraph 15 of their pre-Hearing submission) that a product may under Article 1(b) be a combination of active ingredients. This is also true, but then it must be shown that both the basic patent and the marketing authorisation protect a combination for a request to proceed to grant.

27. To this end, the applicant drew attention to the nature of marketing authorisations, and further to what the authorisation in hand says about the combination of safinamide and levodopa/PDI. They posited that since the MA is expressing a positive right, as opposed to the negative (exclusionary) right of a patent, it should be construed as permissive, and considered in terms of what it enables, rather than its literal scope. However, it is not the place of either a patent examiner or a hearing officer to adjudicate on the purposes of marketing authorisations. Their sole regard in a matter such as this is to whether the identified product corresponds with that in the Request and whether that product is protected by the basic patent submitted in conjunction with it. This is because the SPC is effectively an extension of the *patent* rights for the authorised product. The authorisation rights exist independently of the SPC and have effect without regard to the grant or otherwise of an SPC. For this reason, I cannot accept arguments based on the implicit intent of marketing authorisations, which fall rather under the jurisdiction of those authorities who issue and maintain them. There is also a

compelling legal reason why I cannot accept this argument, to which I will return in a few paragraphs.

28. The applicant further argues that the Yeda (C-518/10) and Yissum (C-202/05) cases, cited by Dr Cassidy in defence of her proposal to reject the SPC request, do not apply because of the particular circumstances of the cases to which their rulings relate. I do not agree with this argument. Matters referred to the CJEU will indeed be referred on the basis of the particulars of the case being heard in the referring national court. However, the questions they refer concern principles of law, and those principles as established by the CJEU in ruling on those questions, apply generally, unless they have been handed down in a specific or limited context. While such cases are heard in the context of the specifics of the referral, the ruling is one of principle and not, unless expressly so limited, particular to the case in question. This is clear from the fact that it is for the referring (national) court to apply the enunciated principle of the CJEU ruling to their original case, and this is not done by the CJEU itself. For this reason, there would need to be very compelling reasons to disapply a CJEU ruling, which I do not find in the submissions of the applicant. Accordingly, I am bound by the principles as ruled in Yeda, Yissum, and indeed all other CJEU rulings, in the absence of a convincing reason that they do not apply.

29. However, I am inclined to the view that Yeda, which

> *preclud[es] the competent industrial property office of a Member State from granting a supplementary protection certificate where the active ingredient specified in the application, even though identified in the wording of the claims of the basic patent as an active ingredient forming part of a combination in conjunction with another active ingredient, is not the subject of any claim relating to that active ingredient alone*

is not relevant to an Art. 3(b) consideration such as the one before me. Yeda is directed to the problem where a single active ingredient forms the product, but the basic patent does not identify that single active uniquely in the patent claims. In the present case, the product for which protection is sought is a combination of safinamide and levodopa/PDI, and each claim of the patent identifies that combination. This issue would certainly have become relevant were the applicant's suggestion that the product identity could be altered to safinamide alone were to have been acted upon, but that is not the case.

30. Yissum, on the other hand is pertinent. In Yissum, the CJEU ruled that

> *Article 1(b) of Regulation No 1768/92 is to be interpreted as meaning that in a case where a basic patent protects a second medical use of an active ingredient, that use does not form an integral part of the definition of the product.*

The applicant argues that Yissum does not apply because the formal decision relates to second medical uses, finding that that aspect of the product is not integral to its identification (that it is not considered in identifying the product). As the applicant observed in the Hearing, the present application relates, at least with respect to safinamide, to a first medical use. (While

this is true from a market authorisation perspective, it is not true from a patent perspective, since I am aware of at least one patent (US2004013620A1) from before the priority date of the basic patent identifying safinamide as an anti-Parkinson's agent. Safinamide has been known as a pharmaceutical since at least 1998 (see Pevarello. P, Varasi M. et al., *Journal of Medicinal Chemistry* **1998** *41* (4), 579-590.)

31. However, this is to ignore the rationale upon which that formal decision is made. Paragraphs 16 to 18 of that judgment are as follows:

> *16. As laid down in Article 1(b) of Regulation No 1768/92, 'product' means the active ingredient or combination of active ingredients of a medicinal product.*
>
> *17. It is clear from Massachusetts Institute of Technology, and, in particular, from paragraphs 19, 21, 23 and 24 of that judgment, that the concept of 'product' referred to in Article 1(b) of Regulation No 1768/92 must be interpreted strictly to mean 'active substance' or 'active ingredient'.*
>
> *18. It follows that the concept of 'product' cannot include the therapeutic use of an active ingredient protected by a basic patent.*

32. The logic of this ruling is that second medical uses are not relevant to the definition of the product *precisely* because the intended therapeutic use does not define the product for the purposes of Art 1(b). Following this reasoning, it is not necessary, in defining the product, to consider for what purpose the MA has authorised the product, merely the identity of the product authorised (other than the general requirement that the product as authorised does indeed fall within the scope of the basic patent). It is to me self-evident that this principle must hold whether the medical use set out is a first or a subsequent medical use.

33. The applicant has sought at length to argue that the context for the authorisation of safinamide is important. To summarise that argument, since safinamide is authorised for use in a context wherein it is used in conjunction with levodopa/PDI (it is given to patients who are already receiving levodopa/PDI, but who no longer enjoy the full effects of that medication), the authorisation is tantamount to a combination authorisation.

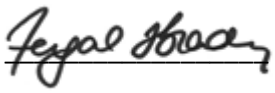
34. Following the logic of Yissum, I cannot accept that argument. It is clear from the authorisation that the only thing authorised to enter the market is safinamide. It (as Xadago®) is the only medicament identified in the Commission's Implementing Decision, and safinamide is the only active constituent of Xadago® identified in Section 2 of the accompanying SmPC.

35. I am therefore bound to find that the marketing authorisation identifies only Safinamide as the product which can be brought to market thereby.

36. That being the case, and having already determined that the basic patent is directed towards the combination of safinamide and levodopa/PDI, this being the product identified in the Request, I must conclude that the marketing authorisation does not extend to the product the subject of the request, since it relates to safinamide alone.

The Decision

37. Accordingly, I find that the product for which the SPC is being sought, being a combination of safinamide and levodopa/PDI, while protected as such by the basic patent in accordance with Art. 3(a), is not the product which is the subject of the marketing authorisation, which is directed solely to safinamide. As such, the Request does not accord with Article 3(b) of Regulation EC 469/2009, and the examiner is correct to have rejected it.



Dr Fergal Brady
Hearing Officer
14 May 2024.