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Datasheet for the decision of 11 June 2024

Case Number: T 0559/22 - 3.3.02

Application Number: 16766424.2

Publication Number: 3344607

IPC: C07D241/20, A61K31/4965, A61P9/10

Language of the proceedings: EN

Title of invention:
SOLID STATE FORMS OF SELEXIPAG

Patent Proprietor:
Teva Pharmaceuticals International GmbH

Opponents:
Chiesi Farmaceutici S.p.A.
HGF Limited

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no)

Decisions cited:
T 1318/21

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Case Number: T 0559/22 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 11 June 2024

Appellant: (Opponent 2)	HGF Limited 1 City Walk Leeds Yorkshire LS11 9DX (GB)
Representative:	HGF HGF Limited 1 City Walk Leeds LS11 9DX (GB)
Respondent: (Patent Proprietor)	Teva Pharmaceuticals International GmbH Schlüsselstrasse 12 8645 Jona (CH)
Representative:	D Young & Co LLP 3 Noble Street London EC2V 7BQ (GB)
Party as of right: (Opponent 1)	Chiesi Farmaceutici S.p.A. Via Palermo, 26/A 43122 Parma (IT)
Representative:	Bianchetti & Minoja with Trevisan & Cuonzo IPS SRL Via Plinio, 63 20129 Milano (IT)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 22 December 2021 rejecting the opposition filed against European patent No. 3344607 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	M. O. Müller
Members:	A. Lenzen
	B. Burm-Herregodts

Summary of Facts and Submissions

I. This decision concerns the appeal filed by opponent 2 (appellant) against the decision of the opposition division (decision under appeal) to reject the opposition against European patent No. 3 344 607 (patent).

II. Reference is made in the present decision to the following documents filed with the opposition division:

D2 US 2014/0155414 A1
D3 Allesø, M. et al., Journal of Pharmaceutical Sciences 97(6), 2008, pages 2145 to 2159
D7 Submission filed during the examination proceedings, dated 20 September 2018
D9 Bavin, M., Chemistry & Industry, 1989, pages 527 to 529
D10 Byrn, S. et al., Pharmaceutical Research 12(7), 1995, pages 945 to 954
D13 European Medicines Agency, Assessment Report: Uptravi

III. With the reply to the statement of grounds of appeal, the patent proprietor (respondent) filed the sets of claims of auxiliary requests 1, 2, 2a, 3, 3a, 4, 4a and 5.

IV. In preparation for the oral proceedings, which had been arranged at the request of both the appellant and the respondent, the board issued a communication pursuant to Article 15(1) RPBA.

V. By letter dated 31 October 2023, opponent 1 announced that it would not be attending the scheduled oral proceedings.

VI. The oral proceedings before the board were held by videoconference on 11 June 2024 in the presence of the appellant and respondent. At the end of the oral proceedings, the chair announced the order of the present decision.

VII. Opponent 1 did not file any requests during the appeal proceedings. The final requests of the appellant and respondent at the end of the oral proceedings were as follows:

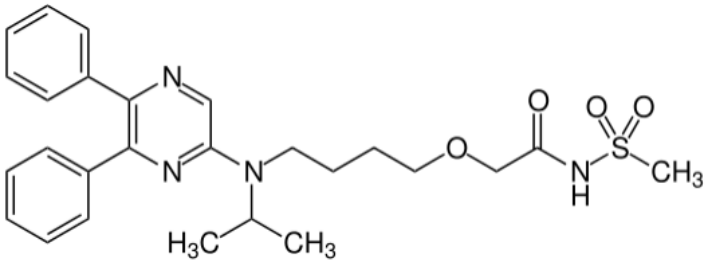
- The appellant requested that the decision under appeal be set aside and that the patent be revoked in its entirety.
- The respondent requested that the appeal be dismissed, implying that the decision under appeal be confirmed and the patent be maintained as granted. In the alternative, the respondent requested that the patent be maintained in amended form based on one of the sets of claims of auxiliary requests 1, 2, 2a, 3, 3a, 4, 4a or 5 (in this order) as filed with the reply to the statement of grounds of appeal.

VIII. Opponent 1 did not provide any comments during the appeal proceedings. Summaries of the appellant's and respondent's submissions, where relevant to the present decision, as well as key aspects of the decision under appeal are set out in the reasons for the decision below.

Reasons for the Decision

Main request (patent as granted) - Inventive step (Article 56 EPC)

1. The patent relates, *inter alia*, to crystalline solid state forms of selexipag. Selexipag has the following chemical structure:



It is intended for the treatment of arteriosclerosis obliterans, pulmonary hypertension and Raynaud's disease secondary to systemic sclerosis (see the patent, paragraphs [0001] to [0003]). Example 3 of the patent describes the preparation of crystalline solid state form IV of selexipag (referred to in the following simply as Form IV), using heptane as the solvent.

2. Claim 1 of the main request reads as follows:

> "*A crystalline form of Selexipag* [sic] *designated as Form IV, characterized by data selected form* [sic] *the group consisting of: an XRPD pattern having peaks at 4.4, 6.6, 12.0, 16.3, and 21.1 degrees 2-theta ±0.2 degrees 2-theta [CuKα radiation (λ = 1.541874 Å)].*"

3. Closest prior art and starting points

3.1 Like the patent, D2 relates to crystalline solid state forms of selexipag (see D2, paragraph [0002], for example). This document was considered to be the prior art closest to the subject-matter of claim 1 of the main request by both the appellant and the respondent. The board saw no reason to take a different view.

3.2 D2 (examples 1 to 5) discloses the preparation of crystalline solid state forms I, II and III of selexipag (referred to in the following simply as Forms I, II and III).

3.3 There was disagreement as to whether only Form I (the respondent's position) or each of Forms I, II and III (the appellant's position) is a suitable starting point for the assessment of inventive step.

3.3.1 According to the respondent, the marketed medicinal product Uptravi® contained Form I (see D13, page 6, second paragraph of the product specification). This meant that Form I had to be considered the more promising form among those disclosed in D2. Moreover, D2 (test examples 2 and 3) disclosed that Form I was advantageous over Forms II and III. Form I could be obtained from the widely available solvent ethanol, it contained less residual solvent and was easier to purify by recrystallisation than Forms II and III. Therefore, the skilled person would not realistically have started from Form II or Form III.

3.3.2 However, as the respondent conceded at the oral proceedings, there is no requirement in the law or elsewhere for the assessment of inventive step to start from those forms of an active pharmaceutical ingredient

(API) which have resulted in a marketed medicinal product. Form I may be superior in some respects to Forms II and III. However, as pointed out by the appellant, D2 clearly sets out its invention as including each of Forms I, II and III (see D2, paragraphs [0009] to [0012]), but only seeks protection for Forms II and III in its claims (see D2, claims 1 and 2), and not for Form I. Therefore, on the basis of D2 it cannot be concluded that Forms II and III are disadvantageous compared to Form I. In light of its claims, D2 rather suggests the opposite.

3.3.3 In summary, there is no reason to assume that the skilled person would not realistically have started from Form II or Form III. Each of Forms I, II and III of D2 is a suitable starting point for the assessment of inventive step.

4. Distinguishing feature(s)

The subject-matter of claim 1 of the main request differs from the individual Forms I, II and III of D2 in that it relates to a different solid state form (characterised by specific XRPD peaks).

5. Technical effect

5.1 There was agreement between the appellant and the respondent that Form IV as disclosed in example 3 of the patent is in accordance with claim 1 of the main request.

5.2 Thus, in order to derive a technical effect for the subject-matter of claim 1 of the main request, Form IV must be compared with Forms I, II and/or III of D2.

According to established case law and contrary to the views of the respondent and the opposition division, the burden of proof in this respect lies at least initially with the respondent (Case Law of the Boards of Appeal of the European Patent Office, 10th edition, 2022, I.D.4.3.1).

5.3 In terms of the effect relevant to inventive step, the respondent relied on higher solubility.

5.4 It was undisputed between the appellant and the respondent that Form IV shows a higher solubility than Form I in aqueous buffer with a pH of 6.8 (see D7, last page).

However, as set out by the appellant, the respondent did not provide any comparison of Form IV with Form II or Form III.

5.5 In the decision under appeal (see page 11, second paragraph), the opposition division stated that Form I had resulted in a marketed medicinal product, but Forms II and III had not. Since the solubility of an API was an important property, it could be concluded that Form I must have a higher solubility than Forms II and III. It followed that the solubility of Form IV must be higher than that of Form I and also higher than that of Forms II and III.

The board does not share this view. Although the solubility of a crystalline solid state form is an important property, it is by no means the only one to be taken into account in the development of a marketed medicinal product. Therefore, the fact alone that a crystalline solid state form resulted in a marketed medicinal product does not necessarily mean that this

form has a higher solubility than any prior-art form which did not result in a marketed medicinal product (i.e. Forms II and III in the present case). The opposition division's conclusion that Form I has a higher solubility than Forms II and III is also not supported by D13, which relates to the marketed medicinal product at issue, Uptravi®. D13 not only contains no information at all on the solubility of Forms I, II and III, but also describes - as submitted by the appellant and not disputed by the respondent - Form I as thermodynamically more stable than Forms II and III. Since higher thermodynamic stability is associated with lower solubility, Forms II and III would be expected to have a higher solubility than Form I.

On the basis of the above considerations alone, it is not convincing that Form I has a higher solubility than Forms II and III. It was therefore not necessary to decide at the oral proceedings on the admittance of the appellant's submission that the particle sizes disclosed in D2 for Forms I, II and III allowed the same conclusion.

As a consequence, the fact that Form IV according to claim 1 of the main request has a higher solubility than Form I does not mean that the solubility of Form IV is also higher than that of Forms II and III.

6. Objective technical problem

6.1 Thus, starting from Form II or III, the objective technical problem is merely to provide an alternative crystalline solid state form of selexipag.

6.2 The fact that the objective technical problem may have to be formulated more ambitiously when starting from Form I (see above; Form IV according to claim 1 of the main request has a higher solubility than Form I of D2) is not decisive in the present case. This is because, as explained above, Form I, Form II and Form III are all possible starting points and the subject-matter of claim 1 of the main request must involve an inventive step starting from each of these forms for an inventive step to be acknowledged.

7. Obviousness

7.1 As set out by the appellant, the skilled person looking for alternative crystalline forms routinely screens for crystalline solid state forms of an API (see D9, page 528, first column, first paragraph; D10, page 946, second column, last paragraph), and during such a screening they examine solvents commonly used for this purpose, such as heptane (see D3, table 1, entry 149). During such a routine screening, the skilled person would have identified Form IV, which is prepared in the patent using heptane as the solvent.

7.2 Contrary to the respondent's argument, in order to deny inventive step the prior art does not have to provide an incentive to use heptane as the solvent - at least not in the present case, where the objective technical problem is merely to provide an alternative crystalline solid state form (see T 1318/21, for example, point 10.2 of the Reasons).

7.3 The respondent argued that D9 and D10 had to be put into perspective. D9 and D10 made it clear that screening for crystalline solid state forms should take place in the early development stage, i.e. shortly

after the actual API was discovered. However, this early development stage had to have been completed before the filing of D2. This was evident from the fact that D2 did not deal with the API selexipag itself but with crystalline solid state forms thereof. Hence, it could not be said that Form IV of the patent was the result of a mere routine screening.

The board shares the appellant's view that this is not convincing. It may be that an extensive screening for crystalline solid state forms is carried out in the early development stage, but there is no apparent reason, and none has been put forward by the respondent either, why the skilled person should not carry out further screenings at a later stage, at least when faced with the problem of providing a further crystalline solid state form.

7.4 Therefore, Form IV of the patent and the subject-matter of claim 1 of the main request which encompasses this form do not involve an inventive step. The main request is not allowable.

Auxiliary requests 1, 2, 2a, 3, 3a, 4, 4a and 5

8. Claim 1 of auxiliary requests 1, 2, 2a, 3, 3a, 4, 4a and 5 differs from claim 1 of the main request only in that further analytical parameters are included in each case. These additional analytical parameters do not change the fact that Form IV of the patent is still encompassed by the subject-matter of claim 1 of auxiliary requests 1, 2, 2a, 3, 3a, 4, 4a and 5.

Since Form IV of the patent is not based on an inventive step, the subject-matter of claim 1 of auxiliary requests 1, 2, 2a, 3, 3a, 4, 4a and 5 is not

based on an inventive step either. Auxiliary requests 1, 2, 2a, 3, 3a, 4, 4a and 5 are therefore not allowable.

The board set this out at the oral proceedings and the respondent did not make any further submissions.

9. Due to the fact that auxiliary requests 2, 2a, 3, 3a, 4, 4a and 5 are not allowable, there was no need at the oral proceedings to decide on the appellant's request not to admit them.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

U. Bultmann M. O. Müller

Decision electronically authenticated