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**Datasheet for the decision
of 26 February 2019**

Case Number: T 0059/15 - 3.3.01

Application Number: 09782127.6

Publication Number: 2320902

IPC: A61K31/517

Language of the proceedings: EN

Title of invention:

PHARMACEUTICAL COMPOSITION COMPRISING LAPATINIB

Patent Proprietor:

Ratiopharm GmbH

Opponent:

Wichmann, Hendrik

Headword:

Lapatinib/RATIOPHARM

Relevant legal provisions:

EPC Art. 54(2), 56, 84

EPC R. 115(2)

RPBA Art. 12(4), 15(6)

Keyword:

Requests submitted with the reply to the statement of grounds of appeal - admitted (yes)

Novelty - main request, auxiliary requests 2-4,8 (no)

Clarity - auxiliary requests 1,5-7 (no)

Inventive step - auxiliary requests 9-11 (no)



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Case Number: T 0059/15 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 26 February 2019

Appellant:
(Opponent)

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Decision under appeal:

**Decision of the Opposition Division of the
European Patent Office posted on 5 November 2014
rejecting the opposition filed against European
patent No. 2320902 pursuant to
Article 101(2) EPC**

Composition of the Board:

Chairman A. Lindner
Members: J. Molina de Alba
 M. Blasi

Summary of Facts and Submissions

- I. European patent No. 2 320 902 was granted with nine claims. Granted independent claim 1 reads as follows:

"1. Pharmaceutical composition comprising N-[3-chloro-4-[(3-fluorophenyl)methoxy]-phenyl]-6-[5[[[2-(methylsulfonyl)ethyl]amino]methyl]-2-furyl]-4-quinazolinamine or a pharmaceutically acceptable salt thereof wherein a unit dose of the composition contains 1200 to 1300 mg of the active pharmaceutical ingredient calculated as the free base."

In the following, the compound cited in claim 1 will be referred to by its common name "lapatinib".

- II. The evidence invoked by the parties during the appeal proceedings included the following documents, wherein documents D4, D13, D15 and D32 had been already cited in the opposition proceedings:

D4 TYKERB[®] (lapatinib) product information, March 2007

D13 L. Lachman et al., The Theory and Practice of Industrial Pharmacy, 2nd Edition (1976), Lea and Febiger, 101

D15 US-A-2008/0026067

D32 Assessment Report for Tyverb, European Medicines Agency, Procedure No. EMEA/H/C/795.

D37 European Pharmacopoeia, 5th Edition (2006),
Supplement 5.6, European Directorate for the
Quality of Medicines and Healthcare, 4472

D38 Webster's Ninth New Collegiate Dictionary, 9th
Edition (1991), Merriam-Webster Inc., 170, 882,
and 1313

D39 Declaration of Prof. Weitschies, dated
16 March 2015

E13 WO 2006/113649

III. Revocation of the patent in suit was sought pursuant to
Article 100(b) and Article 100(a) EPC, for lack of
novelty and inventive step.

IV. By its decision, taken at the oral proceedings on
23 September 2014, the opposition division rejected the
opposition.

The division held that the subject-matter claimed in
the patent as granted was novel and inventive over the
content of, *inter alia*, document D4, considered to be
the closest prior art. The invention was also
sufficiently disclosed in the patent.

V. The opponent (appellant) lodged an appeal against this
decision. With its statement of grounds of appeal, it
filed documents D37 to D39 and 15 exhibits accompanying
D39; document E13 was one of the exhibits.

VI. With its reply to the statement of grounds of appeal,
the patent proprietor (respondent) filed 11 claim sets
as auxiliary requests 1 to 11, indicating the
amendments made to claim 1 of each of the requests and

citing their corresponding basis in the application as filed.

Claim 1 of auxiliary request 1 reads as follows:

"1. Pharmaceutical composition comprising a dosage amount of 1200 to 1300 mg per unit dose of N-[3-chloro-4-[(3-fluorophenyl)methoxy]-phenyl]-6-[5[[[2(methylsulfonyl)ethyl]amino]methyl]-2-furyl]-4-quinazoinamine or a pharmaceutically acceptable salt thereof calculated as the free base."

Claim 1 of auxiliary request 2 is based on granted claim 1, with the additional restriction that the pharmaceutical composition is in the form of a syrup, granulates suitable for suspension, pellets suitable for suspension, or a tablet.

Claim 1 of auxiliary request 3 is based on granted claim 1, with the additional restriction that the pharmaceutical composition is in the form of an effervescent tablet, a syrup, granulates suitable for suspension, pellets suitable for suspension, or granulates compressed into a tablet.

Claim 1 of auxiliary request 4 differs from claim 1 of auxiliary request 3 in that the granulates compressed into a tablet are specified to be obtained by dry compaction or wet granulation.

Claim 1 of each of auxiliary requests 5 to 7 differs from granted claim 1 in that the pharmaceutical composition is in the form of a tablet, granulates compressed into a tablet, or granulates obtained by dry compaction or wet granulation compressed into a tablet, respectively.

Claim 1 of auxiliary request 8 is identical to claim 1 of auxiliary request 3, with the exception that the feature "*granulates compressed into a tablet*" has been removed.

Claim 1 of auxiliary request 9 is based on granted claim 1, with the additional restriction that the active pharmaceutical ingredient has a particle size of 1 to 30µm.

Claim 1 of auxiliary request 10 is based on granted claim 1, with the additional restriction that the active pharmaceutical ingredient has a specific surface area of 5 to 10m²/g.

Claim 1 of auxiliary request 11 is based on granted claim 1, with the restrictions of both auxiliary requests 9 and 10.

- VII. In its preliminary opinion, annexed to the summons to oral proceedings, the board informed the parties that it interpreted the claims such that granted claim 1 encompassed any pharmaceutical composition suitable for preparing the unit dose defined in it. As a result of this construction, the dispersible powder or granulate used for the preparation of the tablets disclosed in D4 would anticipate the composition of granted claim 1. The admission of auxiliary requests 1 to 11 and the documents filed by the appellant with the statement of grounds of appeal would be discussed at the oral proceedings.
- VIII. By letter dated 3 December 2018, the respondent informed the board that it would not attend the oral proceedings.

IX. Oral proceedings were held in the absence of the respondent on 26 February 2019.

X. The appellant's arguments, where relevant to the present decision, may be summarised as follows:

Document D39 and its exhibits, one of which was document E13, had to be admitted because they had been filed in response to the arguments held by the opposition division in the appealed decision. Furthermore, the patent cited E13 in paragraph [0006] as prior art, and the respondent was therefore aware of this document.

By contrast, auxiliary requests 1 to 11 were not to be admitted because the respondent had not explained how their amendments rendered the claimed subject-matter novel and inventive. Moreover, the requests were not convergent. Auxiliary request 1, in particular, had been filed for the first time in the appeal proceedings, even though it was intended to deal with an issue already present in the notice of opposition (construction of granted claim 1).

Granted claim 1 had to be construed as referring to a pharmaceutical composition suitable for providing the defined unit dose rather than to a final dosage form consisting of one unit dose only. Based on this interpretation, the composition in granted claim 1 lacked novelty over the bottle of 150 tablets containing 250 mg lapatinib per tablet disclosed in D4.

The wording of claim 1 of auxiliary request 1 was an inadmissible clarification of the language of granted claim 1. In addition, the claim added subject-matter.

The tablets in claim 1 of each of auxiliary requests 2 to 4 lacked novelty over those disclosed in D4 for the reasons explained in relation to granted claim 1 and because, according to D32 (page 7, last lines), the tablets in D4 had been produced by granulation followed by compression.

The objections raised against claim 1 of each of auxiliary requests 2 to 4 also applied to auxiliary requests 5 to 7, respectively.

For assessing inventive step, document D4 was the closest prior art. The skilled person would have arrived at the alternative dosage forms in claim 1 of auxiliary request 8 by applying routine formulation technology. In addition, the particle size and/or specific surface area characterising the compositions in claim 1 of each of auxiliary requests 9 to 11 were obvious in the light of documents D13 and D15.

XI. The respondent's arguments, where relevant to the present decision, may be summarised as follows:

Document D39 and its exhibits neither responded to the appealed decision nor added anything to what had been discussed in the opposition proceedings. So, they should not be admitted.

Claim 1 should be construed as being limited to a unit dose. This was because, within the meaning of Article 69 EPC, claims had to be read in the light of the description, and the patent made clear, in particular in paragraphs [0007] and [0008], that the only technically sensible construction of claim 1 was that it was limited to a unit dose. Under this premise, the

tablets in document D4 did not anticipate the composition in granted claim 1 because they contained only 250 mg lapatinib, which was below the 1200 to 1300 mg required by claim 1; the five 250 mg tablets that, according to D4, had to be administered once daily, could not be regarded as being a unit dose.

XII. The final requests of the parties were as follows:

- The appellant requested that the appealed decision be set aside and the patent be revoked in its entirety. It further requested that documents D37 to D39 and the 15 exhibits accompanying D39, filed with the statement of grounds of appeal, be admitted into the appeal proceedings and that the 11 sets of claims filed by the respondent with its reply to the statement of grounds of appeal as auxiliary requests 1 to 11 not be admitted into the appeal proceedings.

- The respondent requested in writing that the appeal be dismissed or, alternatively, that the patent be maintained in amended form on the basis of any of the claim sets filed with the reply to the statement of grounds of appeal as auxiliary requests 1 to 11. It also requested that documents D37 to D39 and the 15 exhibits accompanying D39 not be admitted into the appeal proceedings.

XIII. At the end of the oral proceedings, the board's decision was announced.

Reasons for the Decision

1. The oral proceedings before the board took place in the absence of the respondent, which had been duly summoned but chose not to attend, as announced with the letter of 3 December 2018. In accordance with Rule 115(2) EPC, the board decided to continue the proceedings in the respondent's absence. Furthermore, pursuant to Article 15(3) RPBA, the board was not obliged to delay any step in the proceedings, including its decision, simply due to the respondent's absence at the oral proceedings. In line with this provision, the respondent was treated as relying on its written case. Hence, the board was in a position to announce a decision at the conclusion of the oral proceedings, in accordance with Article 15(6) RPBA.

The board also notes that the respondent chose not to provide any arguments in respect of how the amendments introduced in the auxiliary requests rendered the claimed subject-matter clear, novel and inventive; aspects to which the board had drawn attention in its preliminary opinion.

2. Admission of auxiliary requests 1 to 11

Auxiliary requests 1 to 11 were filed by the respondent with the reply to the statement of grounds of appeal. Auxiliary request 1 was considered by the board as a legitimate attempt by the respondent to deal with the interpretation of granted claim 1 made by the appellant in the statement of grounds of appeal, and auxiliary

requests 2 to 11 had been already filed in the opposition proceedings as auxiliary requests 1 to 10. Considering that the opposition division had agreed with the respondent's submissions and rejected the opposition, in the opposition proceedings the respondent was compelled to neither file auxiliary request 1 nor discuss auxiliary requests 2 to 11. Hence, the board, exercising its discretion pursuant to Article 12(4) RPBA, decided to admit auxiliary requests 1 to 11 into the proceedings.

3. Admission of document E13

With the statement of grounds of appeal, document E13 was filed as an exhibit to the declaration D39 to show that lapatinib granules for compression into tablets were known on the priority date of the patent in suit. Moreover, the patent cites E13 in paragraph [0006] as prior art disclosing conventional lapatinib formulations for oral administration.

Document E13 was filed by the appellant at the first possible opportunity in response to the appealed decision and was considered by the board as an appropriate reaction to the decision under appeal. In addition, its content should be known to the respondent, as derivable from the citation of document E13 in the patent. Under these circumstances, the board saw no reason to exclude document E13 from the appeal proceedings under Article 12(4) RPBA.

4. Construction of granted claim 1

Granted claim 1 is directed to a pharmaceutical composition comprising lapatinib or a pharmaceutical acceptable salt thereof, wherein a unit dose of the

composition contains 1200 to 1300 mg lapatinib calculated as the free base. The parties disputed whether the unit dose mentioned in the claim is limiting or merely descriptive.

The respondent contended that, under Article 69 EPC, claims should be interpreted in the light of the description, and that a reading of paragraphs [0007] and [0008] of the patent made clear that the invention was directed to the provision of an improved dosage form of lapatinib that contained the daily lapatinib medication in a single unit dose. Hence, claim 1 had to be interpreted as being directed to a single unit dose comprising 1200 to 1300 mg lapatinib calculated as the free base.

The board disagrees. Granted claim 1 is directed to a pharmaceutical composition rather than to a unit dose. Although the claim gives some information on the unit dose of the claimed composition, it cannot be inferred from its wording that the pharmaceutical composition is limited to that unit dose. In this connection, the board notes that, contrary to the respondent's view, the patent description cannot be used to read into the claim a limitation that is not apparent from its wording. Moreover, claiming the pharmaceutical composition from which the unit dose mentioned in claim 1 may be obtained is neither in contradiction with the patent description nor deprived of technical sense. Hence, granted claim 1 has to be read in its broadest meaningful technical sense, as encompassing any pharmaceutical composition suitable for preparing a unit dose of 1200 to 1300 mg lapatinib calculated as the free base.

This claim construction is equally applicable to claim 1 of each of auxiliary requests 2 to 11, which has wording analogous to that of granted claim 1.

5. Novelty - granted claim 1

Document D4 discloses (see section 11) Tykerb[®] tablets, which are film-coated tablets comprising 250 mg lapatinib calculated as free base. The product is presented in bottles of 150 tablets (see section 16).

Having regard to the fact that film-coated tablets such as those disclosed in D4 are necessarily prepared by compression of a powder or granulate, followed by film-coating the resulting tablet, D4 implicitly discloses a powder or granulate suitable for preparing a unit dose containing 1200 to 1300 mg lapatinib calculated as free base, e.g., as suggested by the appellant, by introducing the corresponding amount of (uncompressed) powder or granules into a sachet. Consequently, the composition in granted claim 1 is not novel (Article 54 EPC).

6. Clarity - claim 1 of auxiliary request 1

Claim 1 of auxiliary request 1 was filed by the respondent with the intention to make clear that only a single unit dose was claimed.

In the board's view, however, the wording of claim 1 is ambiguous because, contrary to the respondent's view, a pharmaceutical composition comprising a dosage amount of 1200 to 1300 mg per unit dose is not clearly limited to that unit dose; the composition may well contain multiple unit doses. This would be, for instance, the case of a syrup from which individual doses of 1200 to

1300 mg lapatinib may be dispensed. Hence, claim 1 of auxiliary request 1 lacks clarity (Article 84 EPC).

7. Novelty - claim 1 of each of auxiliary requests 2 to 4 and 8

Examples 1 and 3 of document E13 disclose the preparation of coated lapatinib tablets comprising 250 mg lapatinib calculated as free base, in the following three steps:

i) wet granulating a mixture of lapatinib, a diluent (microcrystalline cellulose) and a binder (povidone);

ii) blending the resulting granulate with a disintegrant (sodium starch glycolate) and a lubricant (magnesium stearate), and compressing the blend into tablets; and

iii) coating the tablets.

It is apparent from these examples that the granulate resulting from step i) is suitable for suspension, since its granules are compressed into tablets together with a disintegrant and a lubricant so that, upon tablet disintegration, the granules are released in the form of a suspension.

Considering that the granulates prepared in examples 1 and 3 of E13 are suitable for suspension and are also suitable for providing lapatinib unit doses of 1200 to 1300 mg calculated as the free base, they anticipate the pharmaceutical composition in claim 1 of each of auxiliary requests 2 to 4 and 8, all of which are

directed to, *inter alia*, lapatinib granules suitable for suspension (Article 54 EPC).

8. Clarity - claim 1 of each of auxiliary requests 5 to 7

Claim 1 of each of auxiliary requests 5 to 7 is directed to lapatinib compositions in the form of a tablet, wherein the unit dose of the composition contains 1200 to 1300 mg lapatinib calculated as the free base. The claim wording does not establish a clear relationship between the tablet and the unit dose. It is therefore uncertain whether the tablet is a unit dose, whether the unit dose may be constituted by more than one tablet, or even whether one tablet could contain more than one unit dose. Hence, the amendments introduced in claim 1 of each of auxiliary requests 5 to 7 lack clarity (Article 84 EPC).

9. Inventive step - claim 1 of each of auxiliary requests 9 to 11

The patent in suit concerns lapatinib compositions which allow for the preparation of unit doses comprising 1200 to 1300 mg lapatinib calculated as the free base. As explained in the context of the main request and auxiliary requests 2 to 4 and 8, such compositions were also disclosed in documents D4 and E13. These documents are therefore regarded as representing the closest prior art.

The compositions in claim 1 of each of auxiliary requests 9 to 11 differ from the ones in D4 or E13 in that lapatinib (or its salt) has a particle size of 1 to 30µm (auxiliary request 9), a specific surface area of 5 to 10 m²/g (auxiliary request 10), or both (auxiliary request 11). D4 and E13 are silent on the

particle size and the specific surface area of lapatinib.

According to the patent in paragraph [0015], the particle size and specific surface area in claim 1 of each of auxiliary requests 9 to 11 provide advantageous properties with respect to, *inter alia*, solubility. In particular, they provide a fast dissolution of compositions containing a high drug load. The problem to be solved by the compositions in claim 1 of each of auxiliary requests 9 to 11 may then be regarded as the provision of lapatinib compositions with a fast dissolution rate.

The board is satisfied that the problem is credibly solved by the claimed compositions, since the particle sizes and specific surface areas defined in claim 1 of each of auxiliary requests 9 to 11 imply that lapatinib is in the form of a powder, and it is generally known in the field of pharmaceutical formulations that the smaller the particle size or the higher the specific surface area, the faster the dissolution rate. Accordingly, it may be expected that powdered lapatinib exhibits a fast dissolution rate. This general knowledge is corroborated by documents D13 and D15:

D13 is a textbook on industrial pharmacy which states on page 101, right-hand column, that the dissolution rate of a drug is directly proportional to its effective surface area and that the surface area varies inversely to its diameter (i.e. particle size). Thus, in order to improve the dissolution rate of poorly soluble drugs, manufacturers produce micronised powders with particle sizes of less than 5 μm to be incorporated into dosage forms. As an example, the document cites sulfadiazine particles of 1 to 3 μm .

D15 is a patent application aimed at improving the solubility of a powder of a slightly soluble drug by increasing its specific surface area (see abstract and paragraph [0001]). In particular, paragraphs [0006] and [0027] of D15 teach that a specific surface area of 9 to 15 m²/g has a dramatically improved solution velocity.

In consequence, D13 and D15 make credible that the lapatinib formulations in claim 1 of each of auxiliary requests 9 to 11 provide a fast lapatinib dissolution rate, but, for the same reason, these two documents also render the claimed compositions obvious.

As a result, the compositions in claim 1 of each of auxiliary requests 9 to 11 are not inventive (Article 56 EPC).

10. Following the above, none of the claim requests on file is allowable.

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:



M. Schalow

A. Lindner

Decision electronically authenticated