BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [ ] To Chairmen and Members
(C) [X] To Chairmen

D E C I S I O N
of 24 October 2000

Case Number: T 0352/97 - 3.3.1

Application Number: 90305389.0

Publication Number: 0399731

IPC: C07D 471/04

Language of the proceedings: EN

Title of invention:
Azaindenes

Patentee:
ZENECA LIMITED

Opponent:
EISAI Co., Ltd.

Headword:
Azaindenes/ZENECA

Relevant legal provisions:
EPC Art. 54(3), 56, 88, 89, 123(2), (3)

Keyword:
"Novelty (yes) - priority right to a part of a generic claim - relevant elements of generic claim have earlier priority date"
"Inventive step (yes) - skilled person would ignore structurally modification taught in the art for different pharmacological activity"

Decisions cited:
T 0002/83, T 0085/87

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0352/97 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 24 October 2000

Appellant: (Opponent)
EISAI
Koishikawa 4-6-10
Bunkyo-ku
Tokyo 112 (JP)

Representative:
Kindler, Matthias, Dr. Dipl.-Chem.
Hoffmann Eitle
Patent- und Rechtsanwälte
Postfach 81 04 20
D-81904 München (DE)

Respondent: (Proprietor of the patent)
ZENECA LIMITED
15 Stanhope Gate
London W1Y 6LN (GB)

Representative:
Tait, Brian Steel
Intellectual Property Department
ZENECA Pharmaceuticals
Merside
Alderley Park
Macclesfield
Cheshire SK10 4TG (GB)

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 16 January 1997 concerning maintenance of European patent No. 0 399 731 in amended form.**

Composition of the Board:

Chairman: A. J. Nuss
Members: R. Freimuth
J. P. B. Seitz

Summary of Facts and Submissions

I. The Appellant (Opponent) lodged an appeal on 25 March 1997 against the interlocutory decision of the Opposition Division, posted on 16 January 1997, which found that the European patent No. 399 731 in the form as amended during opposition proceedings according to the then pending request met the requirements of the EPC.

II. The opposition was based on the grounds of lack of novelty and inventive step and was supported by several documents including:

(1) EP-A-400 974,

(2) EP-A-426 021,

(3) EP-A-420 237,

(4) EP-A-253 310,

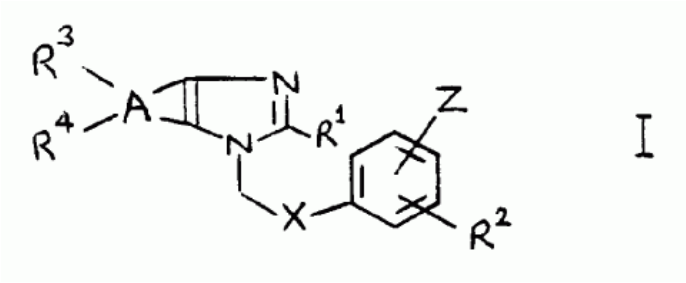
(7) Pharmazie, Vol. 43, pages 315 to 317 (1988),

(8) Drug Development Research, Vol. 8, pages 95 to 102 (1986), and

(9) Yagaku Zasshi, Vol. 94, pages 708 to 716 (1974).

III. The decison was based on an amended first set of ten claims for the Contracting States AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL and SE, independent claim 1 reading as follows:

"1. An azaindene derivative of the formula I



I

wherein A, together with the adjacent vinylene group of the imidazole moiety completes an azene ring selected from pyridine, pyrimidine, pyridazine or pyrazine ring; R^1 is (1-8C)alkyl, (3-8C)cycloalkyl, (3-8C)-cycloalkyl-(1-4C)alkyl, phenyl or phenyl(1-4C)alkyl; R^2 is hydrogen, (1-4C)alkyl, (1-4C)alkoxy, halogeno, trifluoromethyl, cyano or nitro; R^3 and R^4 are optional substituents on the said azene ring, independently selected from hydrogen, (1-4C)alkyl, (3-8C)cycloalkyl, (1-4C)alkoxy, halogeno, trifluoromethyl, cyano, hydroxy, hydroxymethyl, formyl, and nitro; or when A together with the imidazole moiety to which it is attached is an imidazo[4,5-b]pyridine or imidazo[4,5-c]pyridine group, R^3 and R^4; when they are on adjacent carbon atoms of A form a trimethylene or tetramethylene group, or together with the adjacent vinylene group of A complete a benzene ring, the latter optionally bearing a halogeno, (1-4C)alkyl or (1-4C)alkoxy substituent; or when A together with the imidazole moiety to which it is attached is other than a 1H-imidazo[4,5-c]pyridine ring, one of R^3 or R^4 is a carboxy or (1-6C)alkoxycarbonyl group and the other is as defined above; X is phenylene optionally bearing a substituent selected from (1-4C)alkyl, (1-4C)alkoxy and halogeno, or X is a direct bond between the adjacent

phenyl and methylene moieties; and Z is 1H-tetrazol-5-yl or a group of the formula **-CO.OR^5**; or **-CO.NH.SO$_2$.R^6;** in which R^5 is hydrogen or a non-toxic, biodegradable residue of a physiologically acceptable alcohol or phenol, and R^6 is (1-6C)alkyl, (3-8C)cycloalkyl or phenyl; and wherein any of said phenyl moieties may be unsubstituted or bear one or two substituents independently selected from (1-4C)alkyl, (1-4C)alkoxy, halogeno, cyano and trifluoromethyl; or a physiologically acceptable salt thereof except when R^5 is other than hydrogen and R^3 or R^4 is other than carboxy."

The further independent claims 8, 9 and 10 of that first set were directed to a process for the manufacture of the compounds as defined in claim 1, to a pharmaceutical composition comprising a compound as defined in claim 1 and to intermediate compounds according to general formula I wherein a protecting group was affixed to the 1H-tetrazol-5-yl group of the substituent Z, respectively.

The second set of three claims for the Contracting State ES and the third set of four claims for the Contracting State GR were as granted; both comprised an independent process claim identical to claim 8 for the other designated Contracting States and an independent use claim directed to the use of the compounds of formula I, and, for the Contracting State GR, additionally an independent product claim identical to claim 10 for the other designated Contracting States.

IV. The Opposition Division held that the documents cited neither anticipated nor rendered obvious the subject-matter of the patent in suit as amended.

The individual compounds disclosed in documents (1) to (3), which the Opponent used for challenging novelty, were covered by claim 1 of the patent in suit. However, the relevant part of claim 1, i.e. the generic formula as well as the definitions of the substituents given therein which covered those individual compounds, was already described in the first priority document of the patent in suit. To that extent claim 1 was entitled to that first priority date. Documents (1) to (3) having a later priority date, thus, were not novelty destroying pursuant Article 54(3) EPC.

Concerning inventive step the Opposition Division held that, starting from document (4) as closest prior art, the invention aimed at providing further compounds without altering their angiotensin II antagonistic activity. The structural modifications carried out on the known compounds to arrive at the compounds claimed were not rendered obvious by documents (7) to (9) since these were directed to compounds having completely different pharmacological activities.

V. The Appellant argued that the claimed subject-matter was neither novel nor inventive for the reasons being in essence as follows:

A. Documents (1) to (3) disclosed in some examples particular individual compounds representing a specifically selected class of compounds according to formula I wherein the substituent A was a pyridine ring substituted with a methyl group at the 7-position and R^1 a lower (cyclo)alkyl group. Those individual compounds were entitled to priority dates which were situated after the first but before the second priority date of the patent

in suit. Claim 1 of the patent in suit covered those individual compounds; however, that claim was only partially entitled to the first priority date, i.e. only with respect to those elements disclosed in that priority document, pursuant to Article 88(3) EPC. While the first priority document of the patent in suit backed up the generic formula of present claim 1, it neither specified the particular individual compounds disclosed in documents (1) to (3) nor the corresponding particular class of compounds. Hence, the patent in suit was not entitled to the first priority date claimed with regard to those individual compounds. Thus, documents (1) to (3) were prejudicial to the novelty of the subject-matter of claim 1 according to Article 54(3) EPC.

B. Starting from document (4) as closest prior art which taught structurally close compounds having angiotensin II antagonizing activity, the objective problem underlying the patent in suit was the provision of alternative compounds having the same activity. Documents (7) to (9), the compounds thereof having pharmaceutical activity, gave the person skilled in the art the incentive to fuse a 6-membered heterocyclic ring to the imidazol moiety of the compounds known from document (4) thereby arriving without inventive ingenuity at the claimed invention.

VI. The Respondent (Proprietor of the patent) argued that none of the cited documents anticipated the subject-matter of the patent in suit as amended and that none of the cited documents rendered the claimed subject-matter obvious for the reasons being in essence as

follows:

A. Documents (1) to (3) qualified as state of the art pursuant to Article 54(3) EPC only in respect of subject-matter which was entitled to an earlier priority date than the subject-matter of the claims of the patent in suit as amended. In particular, those documents did not qualify as state of the art in respect of the claimed group of compounds which generically or specifically enjoyed the first priority date of the patent in suit since this was the earliest of any priority dates. The disclosure of a generic group in the priority document entitled that particular group to that priority date. The individual compounds of the state of the art referred to by the Appellant were examples within the claimed generic group of compounds which was entitled to that first priority date of the patent in suit. Thus, the disclosure of those individual compounds in documents (1) to (3) claiming later priority dates was not novelty destroying.

B. Starting from document (4) as closest state of the art and aiming at the provision of further compounds having angiotensin II antagonizing activity, the skilled person would not take into account documents (7) to (9) since they addressed different pharmaceutical activities, namely tuberculostatic, antiallergic and hypocholesterolemic activity. Therefore, the claimed subject-matter was not obvious in the light of that prior art.

VII. The Appellant requested that the decision under appeal

be set aside and the patent revoked.

The Respondent requested that the appeal be dismissed.

VIII. Oral proceedings were held on 24 October 2000. At the end of the oral proceedings the decision of the Board was given orally.

Reasons for the Decision

1. The appeal is admissible.

2. *Amendments (Article 123(2) and (3) EPC)*

The amended set of claims for the designated Contracting State AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL and SE as well as the respective sets of claims for the designated Contracting States ES and GR, which are in the form as granted, are those underlying the decision under appeal. No objections pursuant to Article 123(2) and (3) EPC were raised in the decision under appeal against the amended set of claims. In appeal proceedings the Appellant did not challenge in this respect any of the amendments made; nor does the Board see any reason to take a different view since the amendments made to the claims as granted are limited to the removal of two claims and to the deletion of one individual compound from the list given in claim 6.

Thus, that amended set of claims is held to meet the requirements of Article 123(2) and (3) EPC.

3. *Novelty*

3.1 Documents (1) to (3) have been relied on for challenging the novelty of the subject-matter of claim 1 of the amended set of claims for the Contracting States AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL and SE. Those documents were intermediate documents having priority dates situated between the first and the second priority date claimed by the patent in suit. The Appellant and the Respondent had divergent views on the matter of whether or not the disclosure of particular individual compounds in documents (1) to (3) generically covered by present claim 1 were detrimental to the patent's right to its first priority date. Consequently, both parties came to contrary conclusions as to whether or not those documents constitute state of the art pursuant to Article 54(3) EPC destroying the novelty of the subject-matter of claim 1. Therefore, the matter of an effective claim on priority has to be decided by the Board, however, only insofar as it is relevant for the present case.

3.2 The patent in suit claims two priorities, the first dated 23 May 1989 and the second dated 15 March 1990. Document (1) claims the priorities dated 30 May 1989 and 4 May 1990, the former being between the first and the second priority date of the patent in suit. Document (2) claims the priorities dated 31 October 1989, 22 December 1989 and 21 May 1990, the two former being between the first and the second priority date of the patent in suit. Document (3) claims the priorities dated 29 September 1989 and 27 December 1989, both being between the first and the second priority date of the patent in suit. These interpenetrating priority dates of the patent in suit and the addressed documents require the provisions governing priority to be

considered accurately.

3.3 With respect to the purpose of Article 54(3) EPC, the right of priority has the effect that the date of priority counts as the date of filing of the European patent application as prescribed in Article 89 EPC. This effect of the priority right applies to the patent in suit as well as to documents (1) to (3) which are European patent applications.

Whether or not and, if so, to what extent the patent in suit and those documents are entitled to their respective priority dates is governed by Article 88(3) and (4) EPC which states that if one or more priorities are claimed, the right of priority covers only those elements which are included in the application whose priority is claimed, taking into account the application as a whole. In the present case it follows therefrom that the patent in suit as well as documents (1) to (3) may only partially be entitled to a particular priority date, i.e. only for those elements disclosed in the corresponding priority document as a whole. This principle of a partial entitlement to a specific priority date also applies to a single claim since multiple priorities may be claimed for any one claim, i.e. any single claim, pursuant to Article 88(2), second sentence, EPC. Thus, the provisions governing the priority right provide for that present claim 1 for the Contracting State AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL and SE may only partially be entitled to the first priority date claimed.

3.4 Applying these provisions to the present case, a basic consideration is that claim 1, which was challenged by

the Appellant, would have the benefit of the first priority date claimed to the extent that its elements are disclosed in the first priority document of the patent in suit. To the extent that claim 1 enjoys that first priority date, none of the documents (1) to (3) may be considered to be comprised within the state of the art in the sense of Article 54(3) EPC for the simple reason that all those documents claim later priority dates. Only to the extent that some embodiments disclosed in documents (1) to (3) and falling within the scope of present claim 1, would benefit from priority dates earlier than the second priority date of the patent in suit (cf. point 3.2 above) while claim 1 to that extent would not be entitled to the first priority date claimed, those documents would constitute state of the art in the sense of Article 54(3) EPC anticipating the subject-matter of claim 1.

Thus, on the basis of the conclusions indicated above, the embodiments disclosed in documents (1) to (3) as well as the extent to which claim 1 is supported by the first priority date need closer examination.

3.4.1 The Appellant referred in appeal proceedings to the individual compounds disclosed in Examples 9 and 10 of document (1), to the individual compounds No. 1 and 11 disclosed in Example 6 of document (2) and to the individual compounds disclosed in Examples 2, 3 and 5 of document (3) and to the compounds No. 2 to 6 and 11 disclosed in Example 5 thereof, which are 7-methyl-3-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methyl]-3H-imidazo[4,5-b]pyridines having at the 2-position an ethyl, propyl or butyl group or, in the absence of the 7-methyl group, a cyclopropyl group, or which are 4'-

[(7-methyl-3H-imidazo[4,5-b]pyrid-3-yl)methyl]biphenyl-2-carboxylic acids having at the 2-position of the imidazopyridyl ring a methyl, ethyl, propyl, butyl, cyclopropyl or cyclobutyl group.

These individual compounds satisfy the general formula I according to claim 1 of the patent in suit; in terms of that claim, the substituent A represents in these compounds a pyridine ring, R^2 hydrogen, X phenylene and Z 1H-tetrazol-5-yl or -COOH. The individual substituents situated at the 2-position in those compounds fall under the generic definitions (1-8C)alkyl and (3-8C)cycloalkyl alternatively given in claim 1 for the substituent R^1, and those at the 7-position are either hydrogen or fall under the generic definition (1-4C)alkyl, both given in claim 1 for the substituents R^3 and R^4, respectively. Thus, any of those individual compounds disclosed in documents (1) to (3) is generically covered by claim 1 of the patent in suit. This finding has not been contested by the Respondent.

3.4.2 The first priority document GB 8911855 of the patent in suit discloses on page 2, paragraph 2 in combination with page 19 the same general formula I as in present claim 1. The meanings pyridine for the substituent A, hydrogen for R^2, phenylene for X, 1H-tetrazol-5-yl and -COOH for Z, (1-8C)alkyl and (3-8C)cycloalkyl for R^1, and hydrogen and (1-4C)alkyl for the substituents R^3 and R^4 find literal support in that first priority document on page 2, paragraph 2, lines 3 to 11 and 13 to 15.

Therefore those embodiments of claim 1 of the patent in suit having the general formula I and the particular definitions for the substituents A, R^1, R^2, R^3, R^4, X and

Z given above, represent elements within the meaning of Article 88(3) EPC which are entitled to that first priority date. Thus, at least to that extent, claim 1 enjoys the first priority date claimed which is the 23 May 1989. Since any of the documents (1) to (3) merely has the benefit of priority dates after that date (cf. point 3.2 above), they cannot be comprised within the state of the art pursuant to Article 54(3) EPC.

3.4.3 The Board is not convinced by the Appellant's argument that the disclosure of particular individual compounds in documents (1) to (3) referred to in point 3.4.1 above, which were not individually backed up by the first priority document of the patent in suit, though generically covered by present claim 1, was detrimental to that extent to the patent's right to the first priority date claimed resulting in a lack of novelty.

It is established case law of the Boards of Appeal that individual compounds which may be considered as a selection from a general formula, in the present case from general formula I in claim 1 of the patent in suit, and which were specifically disclosed for the first time in documents (1) to (3), do not affect the Respondent-Proprietor's right to the priority date claimed in respect of that general formula as such and its generic elements (see decision T 85/87, point 4 of the reasons, not published in OJ EPO). Since in the present case the relevant elements of claim 1 in the sense of Article 88(3) EPC, i.e. general formula I and the particular, generic definitions for each substituent thereof which are relevant vis-à-vis those individual compounds specifically disclosed in documents (1) to (3), were properly disclosed in the

first priority document of the patent in suit, claim 1, at least to that extent, retains the unreserved benefit of the first priority date claimed, regardless of any further documents in the art entitled to later priority dates.

3.5 In the Board's judgement, therefore, none of the documents (1) to (3) is prejudicial to the novelty of the subject-matter of claim 1 of the set of claims for the Contracting States AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL and SE; nor, by the same token, anticipate those documents any of the further claims thereof which were not objected to by the Appellant.

Nor does the Appellant challenge the novelty of any of the claims of the sets of claims for the Contracting States ES and GR, respectively. The Board is thus satisfied that the novelty of none of those claims is destroyed.

3.6 For these reasons, the Board concludes that the claimed subject-matter of the patent in suit is novel and meets the requirements of Article 52(1) and 54 EPC.

4. *Inventive step*

4.1 The patent in suit relates to substituted 1-(bi)phenylmethyl-imidazole compounds having angiotensin II antagonizing activity (patent specification page 2, lines 4, 5, 26 and 27). Structurally similar compounds having the same pharmacological activity already belong to the state of the art: document (4), which is the state of the art acknowledged in the specification of the patent in suit on page 2, line 24, refers to compounds having the

identical angiotensin II antagonizing activity (page 1, lines 13 and 14). That prior art document discloses imidazole compounds substituted at the 1-position with a carboxy substituted biphenylmethyl group.

The Board considers, in agreement with the Appellant, the Respondent and the Opposition Division, that this disclosure of document (4) represents the closest state of the art, and, hence, the starting point in the assessment of inventive step.

4.2 In view of this state of the art, the problem underlying the patent in suit as submitted by the Respondent and acknowledged by the Appellant consists in providing further compounds having angiotensin II antagonizing activity.

4.3 The patent in suit proposes as the solution to this problem the compounds with the general formula I (see point III above) which are essentially characterized by the presence of an azene ring fused to the imidazole ring.

4.4 The specification of the patent in suit demonstrates on page 6, line 6 to page 7, line 20 by way of a test report that the claimed compounds achieve an angiotensin II antagonizing activity, i.e. solve the problem defined above. Several tests were carried out *in vitro* and *in vivo* and the results indicated show that the angiotensin II activity is antagonized due to the presence of a claimed compound according to general formula I.

For these reasons, the Board is satisfied that the problem underlying the patent in suit has been

successfully solved. This finding has not been challenged by the Appellant.

4.5 Finally, it remains to be decided whether or not the proposed solution to the problem underlying the patent in suit is obvious in view of the cited state of the art.

4.5.1 Document (4), i.e. the closest prior art document (see point 4.1 above), is directed to unfused 1-biphenylmethyl-imidazole compounds having angiotensin II antagonizing activity. It does not give any incentive to structurally modify the imidazole ring by fusing it with an azene ring in order to provide further compounds showing that pharmacological activity. Thus, document (4), on its own, does not render obvious the solution proposed by the claimed invention.

4.5.2 Documents (7) to (9) refer to imidazole compounds wherein an azene ring is fused to the imidazole ring, having pharmacological activities. However, it is to be noted that the compounds of document (7) are reported to show tuberculostatic activity, those of document (8) to show antiallergic activity and those of document (9) to show hypocholesterolemic activity which are pharmacological activities substantially different from and unrelated to that of the present invention, i.e. to antagonize the action of angiotensin II. Therefore, a person skilled in the art would not take the teaching of those documents into consideration at all when looking for a solution to the problem underlying the patent in suit of providing further compounds having angiotensin II antagonizing activity.

The Appellant's objection of obviousness based on documents (7) to (9) leaves aside the established jurisprudence of the Boards of Appeal that, when assessing inventive step, the decisive question is not whether the skilled person **could** have arrived at the invention, in the present case by fusing an azene ring to the imidazole ring, but whether he **would** have done so with the reasonable expectation of providing compounds having angiotensin II antagonizing activity (see for example decision T 2/83, OJ EPO 1984, 265, point 7 of the reasons). Thus, as is clear from the preceding considerations, the latter condition has not been met since the decisive fact remains that documents (7) to (9) are directed to compounds having different pharmacological activities.

Hence, the skilled person would ignore documents (7) to (9) when aiming at a solution to the problem underlying the patent in suit.

4.5.3 To summarise, in the Board’s judgement, none of the documents addressed above renders the claimed invention obvious, either taken alone or in combination.

The Appellant not relying on further documents in order to support his objection of obviousness, the Board is satisfied that none of the other documents in the proceedings renders the proposed solution obvious.

4.6 For these reasons, the Board concludes that the subject-matter of claim 1 of the set of claims for the Contracting States AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL and SE, and, by the same token, that of dependent claims 2 to 7, that of independent claim 8 directed to a process for the manufacture of the

compounds as defined in claim 1, that of independent claim 9 referring to a pharmaceutical composition comprising a compound as defined in claim 1 and that of independent claim 10 directed to intermediate compounds according to general formula I, as well as the subject-matter of any of the claims of the sets of claims for the Contracting States ES and GR, respectively, involve an inventive step within the meaning of Articles 52(1) and 56 EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

N. Maslin A. Nuss