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) [ ] No distribution

D E C I S I O N
of 19 December 2005

Case Number: T 0122/03 - 3.3.04

Application Number: 95927228.7

Publication Number: 0769956

IPC: A61K 38/00

Language of the proceedings: EN

Title of invention:
Use of a GnRH antagonist for the preparation of a medicament for the treatment of gonadal-steroid conditions

Patentees:
Eastern Virginia Medical School
Ortho Pharmaceutical Corporation

Opponent:
Zentaris GmbH

Headword:
GnRH antagonists/EASTERN VIRGINIA MEDICAL SCHOOL

Relevant legal provisions:
EPC Art. 56

Keyword:
"Main and auxiliary request - inventive step (no)"

Decisions cited:
-

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0122/03 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 19 December 2005

Appellant I: (Patent Proprietors)
Eastern Virginia Medical School
358 Mowbray Arch
Norfolk, VA 23507 (US)

and

Ortho Pharmaceutical Corporation
U.S. Route 202 P.O. Box 300
Raritan, New Jersey 08869-0602 (US)

Representative:
Grund, Martin
Dr. Volker Vossius
Patentanwaltskanzlei - Rechtsanwaltskanzlei
Geibelstrasse 6
D-81679 München (DE)

Appellant II: (Opponent)
Zentaris GmbH
Weismüllerstrasse 45
D-60314 Frankfurt/Main (DE)

Representative:
Wibbelmann, Jobst
Wuesthoff & Wuesthoff
Patent- und Rechtsanwälte
Schweigerstrasse 2
D-81541 München (DE)

Decision under appeal:
Interlocutory decision of the Opposition Division of the European Patent Office posted 26 November 2002 concerning maintenance of European patent No. 0769956 in amended form.

Composition of the Board:

Chair: U. Kinkeldey
Members: B. Claes
R. Moufang

Summary of Facts and Submissions

I. European patent No. 0 769 956 with the title "Use of a GnRH antagonist for the preparation of a medicament for the treatment of gonadal-steroid conditions" was granted with 10 claims.

Claim 1 of the patent as granted read:

"1. The use of a GnRH antagonist for the preparation of a pharmaceutical composition for the therapeutic management of a gonadal-steroid dependent condition in a mammal by reducing the estrogen supply in an amount effective to inhibit proliferation of endometrial tissue without substantially stopping the production of endogenous estrogen."

Claims 2 to 10 were dependent on this claim. Claims 8 and 10 read:

"8. The use according to claim 1 wherein the GnRH antagonist is provided in an amount which is effective to provide an average 24 hour serum estradiol from about 30 to 50 pg/ml."

"10. The use according to any one of claims 1 to 9 for the treatment of endometriosis and leiomyomata."

II. After the patent had been opposed in its entirety on the grounds of Article 100(a) EPC concerning novelty and inventive step and that the patentability was excluded by virtue of Article 52(4) EPC, the Opposition Division maintained the patent in amended form, based

on the claims of a first auxiliary request (Article 102(3) EPC).

Claim 1 of the first auxiliary request before the opposition division, a combination of the subject-matter of claims 1, 8 and 10 as granted, read:

"1. The use of a GnRH antagonist for the preparation of a pharmaceutical composition for the therapeutic management of a gonadal-steroid dependent condition in a mammal by reducing the estrogen supply in an amount effective to inhibit proliferation of endometrial tissue without substantially stopping the production of endogenous estrogen, wherein the GnRH antagonist is provided in an amount which is effective to provide an average 24 hour serum estradiol from about 30 to 50 pg/ml for the treatment of endometriosis and leiomyomata." (emphasis added by the board)

III. The patent proprietors (appellant I) as well as the opponent (ASTA Medica AG; original appellant II) have appealed the decision, and submitted a statement of grounds of appeal.

During the appeal proceedings, appellant II asked to register a change of opponent and informed the board that the original opponent (ASTA Medica AG) had transferred the part of its business which related to drug discovery and bioactive substances and to which the present opposition pertained, to Zentaris AG and that thereafter Zentaris AG was merged into Blitz F02-570 GmbH, the name of which was later changed into Zentaris GmbH. Evidence was submitted. Appellant I did

not raise any objection to the alleged transfer of opponent status to Zentaris GmbH.

IV. With a letter dated 30 July 2004 third party observations pursuant to Article 115 EPC were filed concerning the patentability of the claimed subject-matter.

V. Oral proceedings took place on 19 December 2005.

Appellant I requested that the decision under appeal be set aside and that the patent be maintained as granted, or as auxiliary request, that the appeal of appellant II be dismissed. Appellant II requested that the decision under appeal be set aside and that the patent be revoked.

VI. The following documents are referred to in the present decision:

(1) Gordon *et al.* (1992), In "*Modes of Action of GnRH and GnRH Analogs*", Crowley & Conn (Eds.), Springer-Verlag New-York, Inc, p. 332-346.

(4) Barbieri (1992), Am. J. Obstet. Gynecol., 166(2), p. 740-745.

(8) Gordon & Hodgen (1991), Ann. NY Acad. Sci., 626, p. 238-249.

VII. The arguments of appellant I in so far as they are relevant to the present decision may be summarised as follows:

Main request

- Document (4), in the paragraph bridging pages 742 and 743, merely speculated on the existence of a therapeutic window for the concentration of circulating estradiol in the treatment of a gonadal-steroid dependent condition (i.e. "*may exist*"), in particular endometriosis. The same passage expressed doubts whether such a therapeutic window existed in every woman or may be extremely narrow in some women so that it would be difficult to target the estradial concentration to stay within the window. Document (4) at page 744, last paragraph, stated furthermore that the major question was still unresolved which precise concentration of estradiol was required to produce atrophy of endometriotic lesions. Accordingly, document (4) did not teach the skilled person that a therapeutic window of an average 24 hour serum estradiol from about 30 to 50 pg/ml existed, but conveyed complete unclarity whether reducing the estradiol levels to a certain range would have an influence on all endometriotic lesions and whether this certain range was present in all women or could be therapeutically targeted at all.

- The mere speculation and unclarities expressed in document (4) on the existence of a therapeutic window took the skilled person any motivation to search for alternatives to the GnRH agonist used for the adjustment of such a therapeutic window. This was in particular true for regimen III relating to the titration of an GnRH agonist for achieving an

endogenous estradiol concentration within the indicated therapeutic window.

- Of the four treatment regimens with GnRH agonists disclosed in document (4) three concerned a so-called "add-back" therapy, whereby the circulating gonadal-steroid was provided by external administration. Only one regimen, i.e. regimen III, concerned the adjustment of the circulating estradiol concentration by means of the GnRH agonist. Document (4) itself therefore disclosed alternative therapy regimens to the regimen designated regimen III and thus led away from the mere exchange of the GnRH agonist as used for the GnRH antagonist as claimed.

- Regimen III disclosed in document (4) included, prior to the titration of the endogenous estradiol concentration, the administration of a full dose of the GnRH agonist for a time period of three months (see page 743, Figure 5). At least during this time the production of endogenous estrogen had to be considered being stopped. Accordingly, even if the skilled person were to exchange the agonist as used in regimen III for an GnRH antagonist as claimed, the altered therapy would include such a period of frank estradiol deprivation and would therefore not fall under the claim.

Auxiliary request

- The specification of the therapeutic window of circulating estradiol concentration disclosed in document (4) to a range of 30 to 45 pg/ml did not go

beyond the theoretical speculation on the basis of which the existence of such window was suggested.

– Independent claim 1 was directed to a composition "for the treatment of endometriosis and leiomyomata" as opposed to "or leiomyomata". This did not however mean that the patient treated had to suffer from both pathologies.

VIII. The arguments of appellant II in so far as they are relevant for the present decision may be summarised as follows:

Main request

– The closest prior art was represented by document (4). It disclosed the existence of a therapeutic window of the concentration of circulating estradiol for the treatment of endometriosis (see Fig. 2) and a particular treatment regimen III involving the administration of a titrated amount of GnRH agonist for achieving a circulating endogenous estradiol concentration within the therapeutic window (see Fig. 5). The problem to be solved by the subject-matter of claim 1 was therefore the provision of an alternative to the use of the GnRH agonist in regimen III as disclosed in document (4). A number of documents listed a variety of advantages of the use of GnRH antagonists over that of GnRH agonists. Exemplary was the disclosure in document (8) that GnRH antagonists enabled the managing of the degree of diminution of gonadal steroid production, thereby controlling sequelae of severe estrogen deprivation, being important in chronic therapy of gynecologic

problems such as endometriosis and uterine fibroids. The subject-matter of claim 1 was therefore rendered obvious by the disclosure of document (4) read in combination with document (8).

Auxiliary request

- The therapeutic window of the circulating endogenous estradiol concentration aimed for in regimen III disclosed in document (4) was in the range of 30 to 45 pg/ml which fell within the range as specified in claim 1 of the first auxiliary request.

- Independent claim 1 was directed to a composition "for the treatment of endometriosis and leiomyomata" as opposed to "or leiomyomata". One possible interpretation for the use of the "and" operator in this feature of claim 1 was therefore that the treatment was for patients suffering from both diseases. However, a technical problem in the context of such a double treatment was not solved by the patent. Therefore the claimed subject-matter lacked inventive step.

Reasons for the Decision

1. The appeals are admissible.

In view of the information and evidence submitted by appellant II (see above, section III), the board is satisfied that Zentaris GmbH has acquired the status of opponent in the present proceedings: in accordance with the principles in G 4/88 (OJ EPO 1989, 480) the

transfer of the relevant business in the interest of which the present opposition was filed also implied the transfer of opponent status from the original opponent (ASTA Medica AG) to Zentaris AG. Thereafter Zentaris GmbH, being the legal successor of Zentaris AG due to a merger, acquired the opponent status from the latter company.

2. As set out below, the subject-matter of claim 1 of the main and the first auxiliary request is not inventive and thus, the board sees no need to give reasons concerning the issue of novelty (Article 54 EPC).

3. For assessing whether or not a claimed invention meets the requirements of Article 56 EPC, the boards of appeal consistently apply the "problem and solution" approach, requiring as a first step, prior to the formulation of the technical problem to be solved by the invention as claimed, the identification of the closest prior art. In accordance with established case law of the boards of appeal the closest prior art is generally a teaching in a document conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant technical features in common, i.e. ideally requiring the minimum of structural modifications to arrive at the claimed invention.

Main request

4. The subject-matter of claim 1 concerns the therapeutic management of a gonadal-steroid dependent condition in a mammal (such as endometriosis and leiomyomata; see claim 10), by reducing the estrogen supply in an amount

effective to inhibit proliferation of endometrial tissue without substantially stopping the production of endogenous estrogen. This is achieved by the use of a GnRH antagonist.

Paragraph [0008] of the patent indicates as the basis for the claimed subject-matter the recognition that unlike the GnRH **agonist** products, GnRH **antagonists** monopolise the GnRH receptors by competitive occupancy thereby achieving differential degrees of inhibition which are dose dependent. It is therefore possible with the administration of the appropriate dose of GnRH antagonist to maintain tonic ovarian estradiol secretion at a modest level being sufficiently reduced to control the estrogen-dependent gynecological problems, but which are still high enough to avoid the long term sequelae of frank estrogen deficiency. The patent refers especially and explicitly to accelerated bone density loss as a cumulative estrogen-depletion side-effect of a prolonged hypoestrogenic status, such as caused by frank estrogen deficiency among women of reproductive age (see patent paragraph [0006]). Accordingly, the therapeutic management of claim 1 concerns the establishment of a tonic ovarian estradiol secretion level resulting in a circulating endogenous estrogen concentration within a so-called "therapeutic window".

5. The parties have considered either of the teachings in document (1) or (4), which both deal with hormone treatments of gonadal-steroid dependent conditions such as endometriosis, to represent the closest prior art. Whereas document (1) in the sentence bridging page 338 and 339, suggests in a general manner that "*it may be*

practical to titer the dosage of GnRH antagonists such that control of endometriotic implants is achieved without the need for absolute suppression of estrogen concentrations", the author of document (4) explicitly elaborates on the existence of a therapeutic window of estradiol concentration in the context of endometriotic lesions and the practical applications thereof in their treatment. The board therefore considers document (4) to represent the closest prior art for the assessment of inventive step in the present case.

5.1 Starting at page 742, right hand column line 21, document (4), states that "*the basic tenant of the estradiol treshold hypothesis is that tissues vary in their sensitivity to estradiol (Fig. 1). Bone and calcium metabolism may be very sensitive to estradiol, whereas many endometriotic lesions are somewhat less sensitive to estradiol. This difference in estradiol sensitivity means that an estradiol therapeutic window may exist (Fig. 2). At estradiol concentrations of less than 20 pg/ml, endometriotic lesions will tend to atrophy, but loss of bone mineral density will be substantial. At estradiol concentrations of greater than 100 pg/ml, endometriotic lesions will flourish, but loss of bone mineral will not occur.* ***At estradiol concentrations of 30 to 45 pg/ml, many endometriotic lesions may not be stimulated to grow, and bone loss may be minimal"*** (emphasis added by the board). Document (4) then continues: *"Whether an estradiol therapeutic window exists in every woman is unclear. An occasional endometriotic lesion may be extremely sensitive to the stimulatory effects of estradiol. In addition, the "width" of the window may vary from woman to woman. In some women, the window may be extremely narrow, and it*

may be difficult to target the circulating estradiol concentration to stay within the estradiol therapeutic window."

5.2 Based on the foregoing "threshold hypothesis", and with a view to avoid long term sequelae of frank estrogen deficiency, in particular loss of bone mineral density, the author of document (4) describes four GnRH analog administration regimens that were used in long-term hormonal treatment of endometriosis. The GnRH analog used in the regimens are GnRH agonists. Whereas regimens I, II and IV concern so-called "add-back regimens", also referred to in paragraph [0006] of the patent, regimen III (see document (4) page 744, right hand column, first full paragraph), describes as a novel approach to this "add-back", to "***adjust the dose of GnRH analog to allow the ovary to produce enough estradiol to achieve a circulating estradiol concentration in the range of 30 to 45 pg/ml***. *In regimen III, full-dose GnRH analog treatment (e.g. nafarelin nasal solution, 200 µg twice daily) is used for 3 months. The dose of the GnRH analog is then adjusted to produce the desired circulating estradiol concentration. Previous studies suggest that a dose-response relationship exists between nafarelin and circulating estradiol."* (emphasis added by the board)

5.3 Accordingly, regimen III as disclosed in document (4) concerns the therapeutic management of endometriosis by reducing, by means of a GnRH agonist, the estrogen supply in an amount effective to inhibit proliferation of endometrial tissue without substantially stopping the production of endogenous estrogen, thereby avoiding bone mineral density loss.

6. Starting from the teaching of treatment regimen III in document (4), the technical problem to be solved may thus be identified as the provision of an alternative compound to the GnRH agonist in a treatment regimen of a gonadal-steroid dependent condition, such as endometriosis, thereby allowing the ovary to produce a circulating estrogen level within the therapeutic window described. The subject-matter of claim 1 solves this problem by applying GnRH antagonists.

7. Document (4) itself neither suggests nor leads the skilled person away from the claimed solution. In fact, in the latter context, the board notes that the add-back treatment regimens I, II and IV as disclosed in document (4) do not constitute solutions to the formulated technical problem seeing that in these regimens the ovary is not allowed to produce a circulating estrogen level within a therapeutic window, but is rather prevented from producing any estrogen, thereby stopping the production of endogenous estrogen.

8. Consequently, the question to be answered is whether or not any of the other prior art suggested GnRH antagonists as an obvious alternative to the GnRH agonist used in regimen III disclosed in document (4).

9. There is a number of cited prior art documents on file describing the application of both GnRH agonists and antagonists in the treatment of gonadal-steroid conditions such as endometriosis or uterine fibroids, thereby elaborating on potential advantages of GnRH antagonists over GnRH agonists in such context. The board considers document (8) to constitute the most

pertinent of these documents. Document (8) reports on these advantages in the paragraph bridging pages 240 and 241. In particular at page 241, lines 1 to 5, document (8) describes "*the possibility, when using GnRH antagonists, of managing the degree of diminution of gonadal steroid production, thereby controlling sequelae of severe estrogen deprivation, as suggested by preliminary data. (This feature may be important in chronic therapy of gynecologic problems such as endometriosis or uterine fibroids)*".

10. From the above disclosure in document (8) the board concludes that at the relevant date of the patent the skilled person had not only been aware of the alternative applicability of GnRH antagonists and GnRH agonists in the treatment of gonadal-steroid dependent conditions, including endometriosis and uterine fibroids, an alternative denomination for leiomyomata, but had also been informed by the prior art that when such GnRH antagonists were used in such treatment they enabled advantageously the management of the degree of diminution of gonadal steroid production, and therefore of sequelae of estrogen deprivation in comparison to when GnRH agonists were used. Hence, the alternative use of GnRH antagonists over the agonists described in regimen III as disclosed in document (4) is to be regarded as having been obvious to a skilled person.

11. Appellant I has argued that document (4) was highly speculative concerning the existence of a therapeutic window for the treatment of gonadal-steroid dependent conditions such as endometriosis and would therefore take the skilled person any motivation to exchange the

disclosed GnRH agonist in the disclosed regimen for the GnRH antagonist as applied in the claimed invention.

11.1 The board notes however that the author of document (4) based his considerations firstly on the so-called threshold hypothesis that "*tissues vary in their sensitivity to estradiol and that a concentration of estradiol (30 to 45 pg/ml) that will partially prevent bone loss may not stimulate endometriotic lesions to grow. Evidence to support the concept that tissues vary in their sensitivity to estradiol has been provided by Chetowski et al.*" (see document 4, page 741, left hand column lines 2 to 8). Furthermore and secondly, the author reports that "*evidence to support the concept that there may be an "estradiol therapeutic window" comes from studies in which surgical oophorectomy plus estrogen add-back was used to successfully treat women with endometriosis*" (see document (4), page 742, left hand column lines 1 to 5). Accordingly, the author of document (4), for postulating the existence of a therapeutic window, based his considerations on previous research and findings reported in the art.

11.2 The board furthermore considers that in formulating the passages referred to at the end of point 5.1 above, the author of document (4) merely gave expression of a routinely cautious approach of the clinician when reporting on new scientific considerations in the present context, taking into account the anticipated variability in patients and target tissue, rather than stating a prejudice against the applicability of the therapeutic window and the threshold hypothesis.

The board therefore considers the disclosure in document (4) not of such nature to make the skilled person reading it to doubt the genuine scientific relevance of the formulated hypothesis and identified therapeutic window. This argument of appellant I, submitted in order to shed doubt on the *prima facie* obviousness of the claimed subject-matter, is therefore not convincing.

12. Appellant I has furthermore argued that even if the skilled person were to exchange the agonist used in regimen III disclosed in document (4) for an GnRH antagonist, the altered therapy would include a three month period of frank estradiol deprivation and would therefore not fall within the realm of the claimed invention.

The board observes, however, that firstly from page 742, right hand column, lines 33 to 35 of document (4) the skilled person can take that "*at estradiol concentrations of 30 to 45 pg/ml, many endometriotic lesions may not be stimulated to grow*" which corresponds, in the board's opinion, to an amount effective to inhibit proliferation of endometrial tissue as required by claim 1. Accordingly, the second part of regimen III disclosed in document (4) is considered to constitute a therapeutic management as defined in claim 1. Furthermore, the board notes that the wording of claim 1, in reference to the therapeutic management, does not explicitly exclude periods during such management in which the production of endogenous estradiol is substantially stopped. For these reasons also this argument of appellant I does not convince the board.

13. For the above reasons, the subject-matter of claim 1 of the main request lacks inventive step.

Auxiliary request

14. Appellant I auxiliarily requested to dismiss the appeal of appellant II (see section V). Consequently, claim 1 contained in the first auxiliary request before the opposition division (see section II) is relevant for this request.

15. Claim 1 of this request specifies the provision of the GnRH antagonist to be in an amount which is effective to provide an average 24 hour serum estradiol from about 30 to 50 pg/ml and the treatment to be for endometriosis and leiomyomata. Concerning the latter feature, the board notes the use of the "and" operator in the wording of the claim as opposed to e.g. the use of the "or" operator in a wording "for the treatment of endometriosis or leiomyomata".

16. During oral proceedings, when hearing them on inventive step, the parties have expressed different opinions on the construction of claim 1 in the context of the medical indication and therefore on the technical characteristics of the subject-matter claimed.

16.1 A first alternative construction was based on the fact that the specification of the patent invariably refers to endometriosis and leiomyomata as **alternative** pathologies to which a therapeutic management involving the reduction of the estrogen supply in an amount effective to inhibit proliferation of endometrial

tissue without substantially stopping the production of endogenous estrogen can be applied (see e.g. paragraph [0010], describing treatment of endometriosis and leiomyomata as "examples"; paragraph [0013] stating that the invention broadly relates to the treatment of gonadal-steriod dependent conditions "such as" endometriosis, uterine leiomyomata etc.). This first alternative construction would therefore provide the "and" operator the quality of an "or" operator.

16.2 A second alternative construction of the claim started from the premise that the treatment was for patients suffering from **both** endometriosis **and** leiomyomata. This second construction alternative was particularly favoured by appellant II during oral proceedings.

16.3 Appellant I on the other hand stated during oral proceedings that claim 1 should rather be more broadly construed, i.e. a third alternative construction, in that the indicated therapeutic management was **"suitable"** for the treatment of both endometriosis and leiomyomata.

17. The board notes that claim 1 of the auxiliary request is the result of the combination of independent claim 1 as granted and claims 8 and 10 dependent thereon. From a procedural point of view claim 1 of the auxiliary request is thus not open to objections under Article 84 EPC.

18. In view of the above referred to alternatives for the construction of claim 1 of the auxiliary request, the question hence arises as to the actual technical

quality of the use of the "and" operator in the wording of said claim.

19. Nevertheless, and in the context of the examination of inventive step of the claimed subject-matter, the board sees no necessity to decide on a single of the above referred to construction alternatives for claim 1 in view of the fact that either construction alternative results in subject-matter lacking an inventive step for the following reasons:

19.1 In the context of the first possible construction alternative of claim 1 the "and" operator was interpreted as an "or" operator.

As can be taken from point 5.1 above, document (4) discloses a treatment regimen III, representing the closest prior art, (i) in the specific context of the treatment of endometriosis and (ii) the therapeutic window of circulating endogenous estradiol concentration resulting from ovarian estrogen secretion aimed for in the range of 30 to 45 pg/ml. Therefore, neither of the two amendments in claim 1 of the auxiliary request over claim 1 of the main request, in the context of the first construction alternative, would contribute to the inventive quality of the subject-matter claimed related to endometriosis, so that the claimed subject-matter would lack inventive step starting from the teaching in document (4) read in conjunction with the teaching of document (8).

19.2 The board notes that for either of the other two construction alternatives as referred to above, the examination of inventive step of the claimed subject-

matter would require the examination of the claimed-subject matter in the context of the treatment of endometriosis **as well as leiomyomata**, whereby the GnRH antagonist is provided in an amount which is effective to provide an average 24 hour serum estradiol from about 30 to 50 pg/ml.

19.2.1 Document (4) on page 741, right hand column, lines 19 to 22, reports that to reduce myoma volume in premenopausal woman by 50%, estradiol concentrations in the range of 15 to 25 pg/ml must be achieved, whereas estradiol concentrations in the range of 30 pg/ml reliably produce regression in endometriotic lesions. The board considers that this passage in document (4) renders it obvious to a skilled person that a circulating estradiol concentration of 30 pg/ml, as required in claim 1 in the context of leiomyomata, will result in a certain degree of regression of the myoma volume, albeit lower than 50%.

Accordingly, the therapeutic endogenous estradiol window indicated in claim 1 of the auxiliary request is, based on the teaching of document (4), in an obvious manner suitable for the treatment of leiomyomata, seeing that a certain degree of regression could be expected. Hence, the subject-matter as construed in either the second or third alternative referred to above lacks inventive step.

19.2.2 For the sake of completeness, the board has nevertheless considered the implications for inventive step of the claimed subject-matter, if the skilled person were convinced upon reading document (4) that a 30 pg/ml circulating estradiol concentration would not

result in any clinical effect on myoma volume. Then document (4) ought to be interpreted to prejudice the skilled person against the applicability of the indicated therapeutic endogenous estradiol window for the treatment of leiomyomata. In such a case, the patent in suit would be required to provide indications that the claimed subject-matter plausibly solved the problem of providing a treatment for leiomyomata when achieving a circulating endogenous estrogen concentration from about 30 to 50 pg/ml. Seeing however, that the patent is devoid of any such indications in this respect, the patent could then not be taken to provide a solution for this problem, which leads to the conclusion of lack of inventive step.

20. In view of the above and therefore independently of the three alternative claim constructions considered, the board judges that the subject matter of claim 1 according to the auxiliary request lacks inventive step.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

Registrar: Chair:

C. Eickhoff U. Kinkeldey