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

Datasheet for the decision of 3 August 2006

Case Number: T 0274/06 - 3.3.02

Application Number: 04003054.6

Publication Number: 1430897

IPC: A61K 31/485

Language of the proceedings: EN

Title of invention:
Opioid formulations having extended controlled release

Patentee:
EURO-CELTIQUE S.A.

Opponent:
-

Headword:
-

Relevant legal provisions:
EPC Art. 83

Keyword:
"Sufficiency of disclosure - yes:
objection not sufficiently substantiated"

Decisions cited:
T 0060/89

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0274/06 - 3.3.02

D E C I S I O N
of the Technical Board of Appeal 3.3.02
of 3 August 2006

Appellant: Euro-Celtique S.A.
122, Boulevard de la Pétrusse
L-2330 Luxembourg (LU)

Representative: Maiwald, Patentanwalts GmbH
Elisenhof
Elisenstrasse 3
D-80335 München (DE)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 10 October 2005 refusing European application No. 04003054.6 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: U. Oswald
Members: J. Riolo
J. Willems

Summary of Facts and Submissions

I. European patent application No. 04 003 054.6 published as EP 1 430 897 was refused by a decision of the Examining Division pronounced at the end of the oral proceedings of 15 September 2005 on the grounds of insufficiency of disclosure under Article 83 EPC.

II. The decision was based on the set of claims of the main request and auxiliary requests 1 to 3, all filed with the appellant's letter dated 12 August 2005.

Independent claim 1 of the main request reads as follows:

"A multi particulate solid oral dosage form comprising a therapeutically effective amount of a hydromorphone salt in a controlled release matrix comprising at least one controlled release matrix material selected from the group consisting of hydrophilic and hydrophobic polymers, digestible long chain hydrocarbons and polyalkylene glycols, and wherein the dosage form provides an in-vitro dissolution rate being substantially independent of pH and, when measured by the USP Paddle or Basket Method at 100 rpm in 900 ml aqueous buffer (pH between 1 .6 and 7.2) at 37° C, is from 12.5 to 42.5% (by wt) hydromorphone released after 1 hour, from 25 to 56% (by wt) hydromorphone released after 2 hours, from 45 to 85% (by wt) hydromorphone released after 4 hours, and greater than 60% (by wt) hydromorphone released after 8 hours, and wherein the dosage form provides a peak plasma level of hydromorphone in-vivo from 2 to 8 hours after

administration of the dosage form and the dosage form is suitable for administration on a once-a- day basis".

Independent claim 1 of auxiliary request 1 reads as follows:

"Use of a controlled release matrix material selected from the group consisting of hydrophilic and hydrophobic polymers, digestible long chain hydrocarbons and polyalkylene glycols for the manufacture of a multi particulate solid oral dosage form comprising a therapeutically effective amount of a hydromorphone salt in a controlled release matrix comprising at least one of said controlled release matrix materials, and wherein the dosage form provides an in-vitro dissolution rate being substantially independent of pH and, when measured by the USP Paddle or Basket Method at 100 rpm in 900 ml aqueous buffer (pH between 1 .6 and 7.2) at 37° C, is from 12.5 to 42.5% (by wt) hydromorphone released after 1 hour, from 25 to 56% (by wt) hydromorphone released after 2 hours, from 45 to 85% (by wt) hydromorphone released after 4 hours, and greater than 60% (by wt) hydromorphone released after 8 hours, and wherein the dosage form provides a peak plasma level of hydromorphone in-vivo from 2 to 8 hours after administration of the dosage form and the dosage form is suitable for administration on a once-a- day basis".

Independent claim 1 of auxiliary request 2 reads as follows:

"A capsule comprising controlled-release-matrix-granules, -spheroids or -pellets comprising about

8.2 % (by wt) hydromorphone hydrochloride and at least one controlled release matrix material selected from the group consisting of hydrophilic and hydrophobic polymers, digestible long chain hydrocarbons and polyalkylene glycols, and wherein the controlled-release-matrix-granules, -spheroids or -pellets provide an in-vitro dissolution rate being substantially independent of pH and, when measured by the USP Paddle or Basket Method at 100 rpm in 900 ml aqueous buffer (pH between 1 .6 and 7.2) at 37° C, is from 12.5 to 42.5% (by wt) hydromorphone released after 1 hour, from 25 to 56% (by wt) hydromorphone released after 2 hours, from 45 to 85% (by wt) hydromorphone released after 4 hours, and greater than 60% (by wt) hydromorphone released after 8 hours, and wherein the capsule provides a peak plasma level of hydromorphone in-vivo from 2 to 8 hours after administration of the capsule and the capsule is suitable for administration on a once-a-day basis".

Independent claim 1 of auxiliary request 3 reads as follows:

"Use of a controlled release matrix material selected from the group consisting of hydrophilic and hydrophobic polymers, digestible long chain hydrocarbons and polyalkylene glycols for the manufacture of a capsule comprising controlled-release-matrix-granules, -spheroids or -pellets comprising about 8.2 % (by wt) hydromorphone hydrochloride and said matrix material, and wherein the controlled-release-matrix-granules, -spheroids or -pellets provide an in-vitro dissolution rate being substantially independent of pH and, when measured by the USP Paddle

or Baskett Method at 100 rpm in 900 ml aqueous buffer (pH between 1 .6 and 7.2) at 37° C, is from 12.5 to 42.5% (by wt) hydromorphone released after 1 hour, from 25 to 56% (by wt) hydromorphone released after 2 hours, from 45 to 85% (by wt) hydromorphone released after 4 hours, and greater than 60% (by wt) hydromorphone released after 8 hours, and wherein the capsule provides a peak plasma level of hydromorphone in-vivo from 2 to 8 hours after administration of the capsule and the capsule is suitable for administration on a once-a-day basis".

III. The following document was cited inter alia during the proceedings before the Examining Division and during the written proceedings before the Board of Appeal:

(2) EP-A-271 193

IV. According to the text of the decision under appeal, the Examining Division was of the opinion that the European patent application did not fulfil the requirements of Articles 83 EPC (all requests) and 123(2) EPC (auxiliary requests 2 and 3).

Having regard to the prior art acknowledged in the application, which mentioned the difficulties in formulating sustained release dosage forms of hydromorphone, and to the fact that the prior art document (2) disclosed controlled release matrix containing hydromorphone having the same ingredients but with a release profile different from the one in the application, the Examining Division considered that the general information relating to controlled release matrix given in the application was not sufficient for

the skilled person to prepare a controlled release matrix having the very specific release profile of hydromorphone referred to in claim 1 of all requests.

Accordingly, all requests were rejected.

Requests 2 and 3 were moreover rejected on the grounds that they contravened the requirements of Article 123(2) EPC, as the subject-matter of these requests restricted to an amount of 8,2% hydromorphone was not disclosed in the application as originally filed.

V. The appellant (applicant) lodged an appeal against this decision.

The appellant held in substance that, even though the application did not contain any experimental examples, the detailed teaching in the description of the application provided the skilled person with sufficient guidance to enable him the manufacture of the particular claimed dosage forms.

VI. The appellant requested in writing that the decision under appeal be set aside and that the case be remitted to the first instance on the basis of the set of claims of the main request, which was before the Examining Division, or of the sets of claims of the first, second or third auxiliary request of 12 August 2005, which were before the Examining Division.

Reasons for the Decision

1. The appeal is admissible.

2. *Main request*

Article 83 EPC.

2.1 The application relates to a multi particulate solid oral dosage form comprising a therapeutically effective amount of a hydromorphone salt in a controlled release matrix comprising at least one controlled release matrix material selected from the group consisting of hydrophilic and hydrophobic polymers, digestible long chain hydrocarbons and polyalkylene glycols.

The dosage form must provide an in-vitro dissolution rate of hydromorphone having the following profile: 12.5% to 42.5% (by wt) hydromorphone released after 1 hour, 25% to 56% (by wt) after 2 hours, 45% to 85% (by wt) after 4 hours, and greater than 60% (by wt) after 8 hours.

Moreover, the dosage form must provide a peak plasma level of hydromorphone in-vivo from 2 to 8 hours after administration of the dosage form which suitable for administration on a once-a- day basis.

The Board observes that a detailed disclosure of the matrix is given on page 19, line 22, to page 22, line 12, of the description.

On these pages, there is a detailed description of specific materials to be used for the matrix (last

paragraph on page 19), with specific melting points and amounts (first two paragraphs on page 20) and relative amounts of matrix materials (page 20, line 32, to page 21, line 4).

Moreover, the second paragraph of page 21 teaches how the release rate can be set by selecting relative amounts of the retardants.

The Board notes also that the application specifies the in-vitro dissolution method to be used to determine the particular in-vitro dissolution rate of hydromorphone according to claim 1 (page 4, lines 9-11 and 30 and 31) and provides tests for the determination of the peak plasma level (examples 5 to 8).

Under these circumstances and in the absence of concrete evidence or experiments to the contrary, it must be concluded that the application as filed fulfils, *a priori*, the requirements of Article 83 EPC.

2.2 The Board does not agree with the Examining Division's findings that the requirements of Article 83 EPC were not fulfilled because it was deemed to be very difficult to achieve controlled-release matrix containing hydromorphone in general and because the specification did not indicate how to make a once-a-day formulation using the same materials as in document (2), which disclosed a twice-a-day controlled release matrix.

In fact, in the light of document (2), which already describes, *a priori*, an efficient method for preparing controlled-release matrix containing hydromorphone, it must be concluded that the first argument is ill-founded.

As to the second argument, the Board shares the appellant's view that there is again, *a priori*, no reason to doubt that the skilled person can modify the formulations provided in document (2) to extend the release and shift the plasma level merely by "trial and error experimentation" using the teaching set out in said document or the one in the present application as they are similar (grounds of appeal, page 9, third paragraph).

In that respect, the Board would, however, point out that, according to the case law of the Boards of Appeal, "the same level of skill has to be applied when, for the same invention, the two questions of sufficient disclosure within the meaning of Article 83 EPC and inventive step within the meaning of Article 56 EPC have to be considered." (see, eg, T 60/89, OJ EPO 6/1992, 268, see especially Reasons, point 3.2.5).

Accordingly, the points raised by the Examining Division are not sufficient to substantiate an objection under Article 83 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance for further prosecution.

The Registrar: The Chairman:

A. Townend U. Oswald