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Datasheet for the decision of 17 March 2015

Case Number: T 1651/11 - 3.3.01

Application Number: 03721414.5

Publication Number: 1485087

IPC: A61K31/4035, C07D209/48, C07C317/28, A61P35/00

Language of the proceedings: EN

Title of invention:
(+)-2-[1-(3-ETHOXY-4-METHOXYPHENYL)-2-METHYLSULFONYLETHYL]-4-ACETYLAMINOISOINDOLINE-1,3-DIONE FOR USE IN TREATING PSORIASIS BY ORAL ADMINISTRATION

Patent Proprietor:
CELGENE CORPORATION

Opponent:
Ratiopharm GmbH

Headword:
Apremilast against psoriasis/CELGENE

Relevant legal provisions:
EPC 1973 Art. 100(c)
EPC Art. 123(2)

Keyword:
Amendments - added subject-matter (yes)

Decisions cited:
G 0003/89, G 0002/10

Catchword:

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Case Number: T 1651/11 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 17 March 2015

Appellant: (Patent Proprietor)	CELGENE CORPORATION 86 Morris Avenue Summit, NJ 07901 (US)
Representative:	Weber, Martin and Graf, Roland Jones Day Rechtsanwälte, Attorneys-at-Law, Patentanwälte Prinzregentenstraße 11 80538 München (DE)
Respondent: (Opponent)	Ratiopharm GmbH Graf-Arco-Straße 3 89079 Ulm (DE)
Representative:	Schiener, Jens Lederer & Keller Patentanwälte Partnerschaft mbB Unsöldstraße 2 80538 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 19 May 2011 revoking European patent No. 1485087 pursuant to Article 101(3)(b) EPC.**

Composition of the Board:

Chairman	L. Bühler
Members:	C. M. Radke
	G. Seufert

Summary of Facts and Submissions

I. The patent in suit relates to the second medical use of the compound (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione or a pharmaceutically acceptable polymorph, salt, solvate or hydrate thereof, for treating psoriasis by oral administration.

This compound is known by the INN (International Nonproprietary Name) apremilast, which name will be used in the following.

II. The opposition sought revocation of the patent in its entirety and was based on grounds under Article 100(a) (alleged lack of novelty and inventive step) and (c) EPC.

III. The documents cited during the opposition proceedings include the following:

(D1) US-A-6 020 358

(D7) Celgene press release "POSITIVE PHASE IIB TOPLINE CLINICAL DATA FOR CELGENE ORAL COMPOUND APREMILAST (CC-10004) REPORTED FOR PATIENTS WITH MODERATE-TO-SEVERE PSORIASIS", referring to the date "Dec. 15, 2009" on the first page, three pages.

IV. The opposition division decided to revoke the patent.

In particular, the opposition division decided that the subject-matter of claims 1-5 of the sole request was not based on an inventive step in view of document (D1).

V. The appeal of the patent proprietor is directed against this decision.

VI. The documents additionally cited during the appeal proceedings include the following:

(D12) Celgene press release "Apremilast ESTEEM Program Meets Primary and Major Secondary Endpoint in Pivotal Phase III Psoriasis", referring to the date "Jan. 7, 2013" on the first page, two pages

(D13) R. M. Poole and A. D. Ballantyne, "Apremilast: First Global Approval", R&D Insight Report, published online on 6 May 2014, 13 pages

(D14) Notification of the European Commission pursuant to Article 297 of the TFEU to Celgene Europe Limited, 16 January 2015, five pages

(D15) "ANNEX I SUMMARY OF PRODUCT CHARACTERISTICS", 48 pages, enclosed with appellant's letter dated 16 February 2015

(D16) T. Tencer et al., "Economic Evaluation of Sequencing Strategies in the Treatment of Moderate to Severe Psoriasis in the United States", EADV 2014, two pages

Revised Annex A, submitted by the appellant under cover of a letter dated 16 January 2013, 16 pages

VII. The present decision is based on the following sets of claims:

- claims 1-5 as granted (main request) and
- claims 1-5 of the auxiliary request filed with the letter dated 19 September 2011.

a) Independent claim 1 of the main request reads as follows:

"1. Use of stereomerically pure (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione or a pharmaceutically acceptable polymorph, salt, solvate or hydrate thereof, for the manufacture of a medicament for use in treating psoriasis, wherein the medicament is prepared for oral administration."

b) The claims of the auxiliary request differ from those of the main request only in that they contain the additional feature "at a daily dose of between 10 and 200 mg per day".

VIII. The appellant's arguments, as far as relevant for this decision, may be summarised as follows:

The subject-matter of claim 1 of the main request is directly and unambiguously disclosed
- in claim 30 which refers to claim 20 via claim 29 and
- in the description as a whole as originally filed.

In particular, the application as originally filed discloses
- oral administration in section 4.3.1 on pages 21-23 and in examples 8 and 10;
- treating diseases and disorders on page 3, lines 22-25, and on page 4, lines 16-18;
- "psoriasis" on page 4, lines 20-30;

Due to the fact that the first sentence of the paragraph on page 4, lines 16-30, is restricted to the treatment

of diseases, the whole paragraph is limited to the treatment of the diseases mentioned therein. The nature of psoriasis is such that it is treated rather than prevented.

As to the auxiliary request, page 21, lines 3-5, of the application as filed only mentions that the doses may differ depending on the route of application. Moreover, the additional feature is based on original claims 30, 34 and 40.

IX. The arguments of the respondent which are relevant for the present decision are the following:

Claim 1 of the main request is an inadmissible selection, i.a.

- of "treating" from the alternatives "treating or preventing" in original claim 20,
- of "psoriasis" from the list of diseases in original claim 20 and
- of oral administration among the different routes of application disclosed in original claim 29 or in sections 4.3.1 to 4.3.4 of the application as originally filed.

The sentence on page 4, lines 16-18, of the application as filed is not limited to treatment but also includes prevention, as is apparent from the next sentence. Therefore, the respective paragraph also refers to the prevention of the diseases listed therein. This is in line with original claim 20 which relates to a method of "treating or preventing" the diseases listed therein.

Prevention of psoriasis means reduction of the inflammation markers before the symptoms show on the skin; such a prophylaxis makes sense. The effective

amount for the treatment of psoriasis may differ from the one necessary for its prevention.

The objection raised against the main request holds even more for claim 1 of the auxiliary request which additionally indicates a range for the daily dose. Page 21, lines 3-15, of the application as filed does not relate to oral administration; page 21, lines 3-5, mentions that the dose may depend on the route of administration.

X. The appellant (patentee) requested that the decision under appeal be set aside and that the patent be maintained as granted, or, alternatively, on the basis of the claims of the auxiliary request filed with the letter dated 19 September 2011.

The respondent (opponent) requested that the appeal be dismissed. Furthermore, it requested that the "Revised Annex A" and documents (D12) to (D16) not be admitted into the proceedings.

XI. At the end of the oral proceedings the chairman announced the decision of the board.

Reasons for the Decision

1. The appeal is admissible.

2. Article 100(c) EPC 1973

2.1 Grounds under Article 100(c) EPC prejudice the maintenance of the patent if "the subject-matter of the European patent extends beyond the content of the application as filed". This corresponds to the requirements of Article 123(2) EPC.

It is settled case law that the claims of a European patent may be amended "only within the limits of what a skilled person would derive directly and unambiguously, using common general knowledge and seen objectively and relative to the date of filing, from the whole of these documents as filed" (G 03/89, OJ EPO 1993, 117, point 3 of the Reasons, affirmed in G 02/10, OJ EPO 2012, 376, point 4.3 of the Reasons).

Main Request

2.2 It was disputed whether or not the subject-matter of claim 1 as granted, i.e. of claim 1 of the present main request, extends beyond the content of the application as filed.

This claim is a Swiss-type claim relating to
- the treatment of
- psoriasis by
- oral administration of apremilast

(see point VIIa) above).

The respondent stated that the application as filed related to
- the treatment or the prevention of
- diverse diseases, one of them being psoriasis (see e.g. original claim 20),
- by means of apremilast in oral, delayed-release, parenteral, transdermal, topical or mucosal dosage forms (see sections 4.3.1 to 4.3.4 of the application as filed).

It concluded that the combination of features of claim 1 was not directly and unambiguously disclosed in the application as filed.

The appellant considered that original claim 30 referring to original claim 20, and the original description as a whole, disclosed these features in combination.

2.2.1 Original claims 30 and 20

Original claim 30 relates to the method of **claim 29** wherein the stereomerically pure apremilast is administered orally.

Original claim 29 is directed to the method of **claim 19 or 20** wherein the stereomerically pure apremilast is administered parenterally, transdermally, mucosally, nasally, buccally, sublingually or orally.

Original claim 20 is directed to a "method of treating or preventing depression, asthma, inflammation, inflammatory skin disease, psoriasis, atopic dermatitis, contact dermatitis, rheumatoid arthritis, osteoarthritis, chronic obstructive pulmonary disease, chronic pulmonary inflammatory disease, inflammatory bowel disease, Crohn's Disease, Bechet's Disease or colitis which comprises administering to a patient in need of such treatment or prevention a therapeutically or prophylactically effective amount of stereomerically pure (+)2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione [apremilast], or a pharmaceutically acceptable prodrug, metabolite, polymorph, salt, solvate, hydrate, or clathrate thereof".

Hence, it has to be assessed whether or not the person skilled in the art using his common general knowledge would directly and unambiguously derive the combination

of features of present claim 1 from this combination of original claims.

As the application as filed deals with the treatment or prevention of the diseases listed in original claim 20, the skilled person will be one whose common general knowledge comprises an at least superficial knowledge of the nature of these diseases.

Although document (D7) was published after the present priority date, the following general information on psoriasis clearly belonged to the general knowledge of the person skilled in the art before the present priority date, as it is merely based on the prominent visual symptoms:

"Psoriasis is [a] ... chronic inflammatory skin disorder of unknown cause. The disorder is a chronic recurring condition which varies in severity from minor localized patches to complete body coverage. Plaque psoriasis is the most common type of psoriasis ... which appears as patches of raised, reddish skin covered by silvery-white scales. These patches, or plaques, frequently form on the elbows, knees, lower back, and scalp" (see page 2, the section "About Psoriasis").

Hence, psoriasis is a chronic disease involving recurring skin disorders. In this context, two types of medication against psoriasis make sense: The first type is prevention, by reducing the inflammation markers which cause the symptoms on the skin (see the penultimate paragraph under point IX above). The second type involves treatment once the symptoms on the skin are beginning to show. As far as this treatment is concerned, topical application of the drug is a valid option at least for less severe cases. Such treatment

involves contacting the affected parts of the skin with the drug. On the other hand, such a topical application of the drug does not necessarily make sense when trying to prevent the symptoms of the disease, e.g. without knowing where patches are likely to turn up.

For this reason, the person skilled in the art might associate the treatment of psoriasis with a mode of application different from its prevention.

Consequently, the skilled person could interpret original claim 30, to the extent that it is dependent on claim 20, that the expression "treating **or** preventing" (emphasis added) in claim 20 is to be read as referring to oral prevention of psoriasis but not to its oral treatment.

Hence, original claim 30, as far as it is dependent on original claim 20, does not clearly and unambiguously disclose oral treatment of psoriasis by means of apremilast.

2.2.2 The description

As mentioned in the third paragraph of point VIII above, the appellant relied on the following parts of the description:

- section 4.3.1 on pages 21-23 and examples 8 and 10 for the oral administration, and
- page 3, lines 22-25, and page 4, lines 16-30, for the treatment of diseases, in particular of psoriasis.

Section 4.3.1 on pages 21-23 bears the heading "ORAL DOSAGE FORMS". Example 8 relates to testing apremilast by means of a lipopolysaccharide-induced ferret model

(see the heading on page 36, lines 8-9, where LPS stands for lipopolysaccharide), example 10 to an oral dosage form, namely a tablet (see page 40, lines 8-12). Neither section 4.3.1 nor examples 8 or 10 mention whether these dosage forms were to be used for the prevention or for the treatment of a disease, nor do these parts of the description refer to any specific type of disease.

As far as page 3, lines 22-25, is concerned, the board concurs with the appellant that the sentence concerned refers to the treatment of diseases and not to their prevention. However, this sentence and the following parts of the description up to page 4, line 15, are silent on psoriasis, let alone on the oral administration of a drug.

The relevant parts of the paragraph at page 4, lines 16-30, read as follows:

"The invention also encompasses the use of the (+) enantiomer of 2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindoline-1,3-dione [apremilast] to **treat** diseases or disorders ameliorated by the inhibition of PDE4. For example, the compounds and compositions of the invention may be useful to **treat or prevent** viral, genetic, inflammatory, allergic, and autoimmune diseases. Examples of such diseases include, but are not limited to: HIV; ...; **psoriasis**; ...; asthma; and hyperoxic alveolar injury" (emphasis added by the board).

The first sentence of this paragraph refers to the treatment of diseases; it does not mention prevention. This is the basis of the appellant's argument that the whole paragraph relates to the treatment and not to the prevention of the diseases listed therein. The

respondent relied on the second sentence of this paragraph, which refers to the treatment or the prevention of certain types of diseases.

The third sentence of this paragraph begins with the words "Examples of such diseases" and thus refers directly to the previous sentence relating to the treatment or prevention of certain types of diseases. Hence, said paragraph discloses the **treatment or prevention of** the numerous diseases, including **psoriasis**, listed in this sentence.

Consequently, the features of present claim 1, namely the treatment of psoriasis by oral application of apremilast, are also not disclosed in combination in the parts of the description the appellant relied on.

2.2.3 Hence, the subject-matter of amended claim 1 as granted extends beyond the content of the application as filed. Therefore, grounds under Article 100(c) EPC prejudice maintenance of the patent on the basis of the main request.

Auxiliary Request

3. Claim 1 of the auxiliary request comprises the same combination of features as claim 1 of the main request. Therefore, the reasons under point 2 above apply *mutatis mutandis* to the auxiliary request. This leads to the conclusion that claim 1 of the auxiliary request likewise contains subject-matter which extends beyond the content of the application as filed. Consequently, claim 1 of this request does not meet the requirements of Article 123(2) EPC.

4. In summary, grounds under Article 100(c) EPC prejudice maintenance of the patent on the basis of the main request. Claim 1 of the sole auxiliary request does not comply with Article 123(2) EPC. The board can only decide on a request as a whole. Therefore, neither the main request nor the auxiliary request is allowable.

5. Respondent's request not to admit documents (D12) to (D16) and "Revised Annex A" into the proceedings

The discussion during the oral proceedings before the board was limited to grounds under Article 100(c) EPC and to the requirements under Article 123(2) EPC; there was no discussion of inventive step. Neither the parties nor the board considered documents (D12) to (D16) and "Revised Annex A" to be relevant for the discussion.

Therefore, there was no need to decide whether or not to admit these documents into the proceedings.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow L. Bühler

Decision electronically authenticated