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**Datasheet for the decision
of 20 February 2020**

Case Number: T 1914/16 - 3.3.01

Application Number: 04766791.0

Publication Number: 1670482

IPC: A61K31/57, A61K31/58, A61K9/00

Language of the proceedings: EN

Title of invention:
USE OF CICLESONIDE FOR THE TREATMENT OF RESPIRATORY DISEASES

Patent Proprietor:
Covis Pharma B.V.

Opponent:
Generics [UK] Ltd (trading as Mylan)

Headword:
Ciclesonide/COVIS

Relevant legal provisions:
EPC Art. 54, 56, 83, 123(2)

Keyword:
main request - allowable



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Case Number: T 1914/16 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 20 February 2020

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Decision under appeal: **Interlocutory decision of the Opposition
Division of the European Patent Office posted on
8 June 2016 concerning maintenance of the
European Patent No. 1670482 in amended form.**

Composition of the Board:

Chairman A. Lindner
Members: M. Pregetter
P. de Heij

Summary of Facts and Submissions

- I. European patent No. 1 670 482 is based on European patent application No. 04766791.0, filed as an international application published as WO2005/025578.
- II. The following documents, cited during the opposition and appeal proceedings, are referred to below:
- (1) Dent G., *Curr Opin Investig Drugs*, 2002, 3(1), 78-83
- (8) Agertoft et al., *J Allergy Clin Immunol*, 2004, 113(2), Suppl., S119
- (14) Weinbrenner et al., *J Endocrinol Metab*, 2002, 87(5), 2160-2163
- (16) Allen D.B., *Pediatr Pulmonol*, 2002, 33, 208-220
- (17) von Berg et al., *Pediatr Allergy Immunol*, 2007, 18, 391-400
- (18) Agertoft et al., *Pediatr Allergy Immunol*, 2009, 1-7
- (21) Pedersen S., *Am J Respir Crit Care Med*, 2001, 164, 521-535
- III. European patent EP 1 670 482 was opposed under Article 100(a), (b) and (c) EPC on the grounds that the claimed subject-matter lacked novelty and inventive step, was not disclosed in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art, and extended beyond the content of the

application as filed. An objection was raised against the validity of the priority.

- IV. In the course of the opposition proceedings, the patent proprietor requested the rejection of the opposition and submitted various auxiliary requests.

The opposition division found that auxiliary request 9 met the requirements of the EPC.

- V. Both the patent proprietor and the opponent filed an appeal against the opposition division's decision.

- VI. On 3 December 2019 the board issued a communication pursuant to Article 15(1) RPBA 2007.

- VII. Oral proceedings before the board took place on 20 February 2020 in the absence of appellant 2 as announced by letter of 14 February 2020.

During the oral proceedings appellant 1 submitted an amended main request and renumbered the former main request to auxiliary request 1 and former auxiliary requests 1 to 11 to 2 to 12, respectively.

Claim 1 of the main request reads as follows:

"1. Use of ciclesonide, a pharmaceutically acceptable salt or solvates thereof for the manufacture of a medicament for the treatment or prevention of asthma in a patient, which patient is a child, while reducing or avoiding growth suppression as the side effect associated with inhaled and intranasal corticosteroids, and wherein the medicament is suitable for administration by inhalation and is administered at a daily dose of 20 to 200µg ciclesonide in a continuous

treatment regimen."

VIII. Appellant 1's arguments, in so far as they are relevant to the present decision, may be summarised as follows.

Amendments

The subject-matter of claim 1 of the main request did not extend beyond the content of the application as filed. The combination of features could be found in claims 22, 34 and 37, and in the description on page 1, first and third paragraphs, page 2, second paragraph, the paragraph bridging pages 2 and 3, page 3, second and fourth paragraphs, and the passages on pages 4 to 7 relating to the formulation and packaging of compositions suitable for inhalation. Both examples supported the combination of the technical features of claim 1.

Clarity and sufficiency of disclosure

Arguments concerning the scope of a claim should not be discussed under the requirement of sufficiency of disclosure.

Priority and novelty

In the present case, a finding of compliance with Article 123(2) EPC entailed entitlement to the priority, thereby removing document (8) from the state of the art according to Article 54 EPC.

Inventive step

The closest prior art was document (16). The difference between the subject-matter of claim 1 of the main

request and document (16) was the active agent. This difference resulted in reduced growth suppression in the treated children. Data supporting this could be found in documents (18) (comparison with fluticasone propionate) and (17) (comparison with budesonide).

The technical problem was the provision of a safer treatment of respiratory diseases in children which did not result in growth suppression.

There was no motivation for the skilled person to consider ciclesonide as solution to this problem. In particular, document (1) did not provide any guidance as it concerned treatment of asthma in adults.

- IX. Appellant 2's arguments, as presented in writing and in so far as they are relevant to the present decision, may be summarised as follows.

Amendments

The claimed subject-matter extended beyond the content of the application as filed. The technical features were not disclosed in combination. The examples could not serve as a basis since they related to short-term reduced leg growth retardation and not to growth retardation in general. Moreover, the examples merely related to doses of 40, 80 and 160 µg ciclesonide. The omission of the term "after long-term exposure" led to an unallowable broadening of the claim that was not derivable from the application as filed. There was no basis for the feature "child" as far as this related to children outside the age group of 6 to 12 years.

Clarity and sufficiency of disclosure

The claims were ambiguous. Claims had to be clear to allow the skilled person to establish the scope of the claim without undue burden. Example 2 showed that at the two higher doses growth suppression did occur. Furthermore, there was no data showing an effect for children outside the age group tested. There was no reason to expect growth suppression after long-term exposure at the stated dosages. Thus the claim was unclear and the invention could not be performed over its whole scope.

Priority and novelty

The new claim sets submitted by appellant 1 required that the appellant 2's submissions with respect to lack of novelty with regard to E8 and priority be reintroduced as during opposition.

Inventive step

The closest prior art was document (16). It was, however, questionable whether long-term exposure resulted in a problem based on growth retardation, especially in the case of ciclesonide. Consequently, a problem-solution approach based on a problem that takes growth retardation into account was flawed. If, however, the "problem" were taken to be the provision of an asthma treatment with a reduced potential for growth suppression in children, the claimed subject-matter was obvious. It was known from document (14) that ciclesonide was safe and had a low systemic availability. Therefore, minimal or no side effects associated with growth suppression were to be expected.

Starting from document (1) as the closest prior art, the only difference with the claimed subject-matter was the patient group. In view of the therapeutic index and properties of ciclesonide described in document (1), the skilled person would have expected ciclesonide to be a suitable candidate for treating asthma in children. Furthermore, document (21) stated that doses of 100 to 200 µg of inhaled corticosteroid were safe. The patent in suit did not demonstrate any effect for children below 6 or over 12 years of age.

- X. Appellant 1's final requests were that the decision under appeal be set aside and that the patent be maintained on the basis of the set of claims of the main request, filed at the oral proceedings of 20 February 2020, or, alternatively, on the basis of the set of claims of one of auxiliary requests 1 to 12, all filed with appellant 1's written submissions.

Appellant 2 had requested in writing that the decision under appeal be set aside, that the patent be revoked and that documents (28) to (40) be admitted into the proceedings.

Reasons for the Decision

1. The appeals are admissible.
2. The oral proceedings before the board took place in the absence of appellant 2, who had been duly summoned but had chosen not to attend. According to Rule 115(2) EPC and Article 15(3) RPBA 2020, the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who is then

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, as provided for by Article 15(6) RPBA 2020.

Main request

3. *Amendments*

3.1 Claim 1 of the main request combines various features from the application as filed. In the following, all references relate to W02005/025578.

In order to arrive at claim 1 of the main request, claim 22 as filed has been combined with either the passage on page 2, first full paragraph, or the paragraph spanning pages 2 and 3.

These passages disclose in general terms that administering ciclesonide in the doses defined in claim 22 to a patient which is a child for the treatment of a respiratory disease avoids the side effect of growth suppression. It is not necessary to include the term "after long-term exposure" in claim 1 of the main request, since this feature has to be considered to be an inherent feature of the treatment (in the present case of the continuous daily administration of a corticosteroid for treating a chronic disease (asthma)) and of the time scale within which growth suppression may be observed.

Treating asthma in children is the preferred treatment in the application as filed; see page 1, first paragraph.

In the context of asthma treatment, the provision of a

medicament comprising ciclesonide as the active agent suitable for administration by inhalation is highlighted as the most preferred embodiment in the application as filed: when discussing the background, ciclesonide is introduced as "a novel inhaled corticosteroid for asthma treatment" (page 1, last paragraph, first sentence). The passage from the second paragraph on page 4 to the fourth paragraph on page 7 describes formulations and devices for inhalation, with the exception of a four-line paragraph in the middle of page 6 which, in a very general way, mentions nasal drops as an alternative to intranasal sprays. Starting on page 8, the disclosure of both examples on file is limited to formulations provided in metered-dose inhalers, indicating administration by inhalation. Thus, inhalation is the preferred administration route.

A continuous treatment regimen involving daily administration of ciclesonide is disclosed in claim 27 as filed (referring directly to claim 22) and on page 3, first full paragraph.

The deletion of the term "physiologically functional derivative" does not extend the subject-matter since ciclesonide is clearly the preferred active ingredient.

The combination of the technical features of claim 1 of the main request is thus directly and unambiguously derivable from the application as filed.

- 3.2 Dependent claim 18 can be derived from the second paragraph on page 3, and defines preferred dosage regimens. Example 2 relates to the same dosage regimens, further stressing the preferred nature of these regimens.

No objections concerning the other dependent claims are on file.

3.3 Appellant 2 has not raised any objections concerning Article 123(3) EPC. The board sees no reason to raise any such objections.

3.4 Consequently, the subject-matter of the claims of the main request fulfils the requirements of Article 123 EPC.

4. *Clarity*

Appellant 2 has not indicated any specific technical feature present in claim 1 of the main request and not present in claim 1 as granted that leads to a lack of clarity. It has not been argued that the introduction of the amended technical features in combination with the features already present in the claim as granted would lead to a lack of clarity. The technical features present in claim 1 as granted are not open to a clarity objection (see decision of the Enlarged Board of Appeal G3/14). Therefore, the question of whether a skilled person can unambiguously determine whether or not they are operating within the scope of claim 1 of the main request is not relevant in the present case.

5. *Sufficiency of disclosure*

Example 2 of the patent in suit shows that the administration of various doses of ciclesonide, covering a broad range of doses, does not lead to significant growth suppression in children aged 6 to 12 years. Appellant 2 has provided no evidence that different results were to be expected for children below 6 or above 12 years of age. The activity of

ciclesonide as a corticosteroid effective in the treatment of asthma was known before the priority date of the patent in suit and has not been contested.

The issue of whether or not the skilled person, on the basis of their knowledge derived from the literature, expects a certain effect to arise is not crucial for sufficiency of disclosure in view of example 2.

The subject-matter of claim 1 of the main request is sufficiently disclosed (Article 83 EPC).

6. *Priority and novelty*

The general reference of appellant 2 to its submissions regarding priority and novelty in first instance does not comply with Article 12(3) RPBA 2007, requiring a party to present its complete case in appeal, and thus to be disregarded. In view of the allowability of the amendments and the fact that the priority document is identical to the application as filed in the relevant passages, the priority is in any case validly claimed.

Consequently, document (8) does not form part of the state of the art according to Article 54(2) EPC.

No further document has been cited as being novelty-destroying.

The subject-matter of claim 1 of the main request is novel (Article 54 EPC).

7. *Inventive step*

7.1 The patent in suit concerns the safe and effective treatment of respiratory diseases, in particular

asthma. Side effects such as growth suppression are intended to be reduced or completely avoided (paragraphs [0001] and [0004]). To this end, the corticosteroid ciclesonide is to be administered at a daily dose of 20 to 200µg in a continuous treatment regimen via a medicament suitable for administration by inhalation.

- 7.2 The decision under appeal identified document (16) as the closest prior art. Document (1) was mentioned as another, albeit less promising starting point. As document (16) concerns the safety of inhaled corticosteroids in children in the context of asthma therapy and identifies growth suppression as a major side effect (abstract), the board also considers document (16) to represent the closest prior art. Appellant 2 has not put forward any further arguments concerning the choice of the closest prior art.

Document (16) reports that administration of corticosteroids via inhalation can affect growth (page 212, left-hand column, first full paragraph). Corticosteroids used in the treatment of asthma in children are beclomethasone dipropionate, budesonide, flunisolide, fluticasone propionate and triamcinolone acetonide (Table 1). Dose-related decreases in the linear growth rate of bone were observed in knemometry studies of children with asthma treated with short courses (2-8 weeks) of inhaled beclomethasone dipropionate and budesonide (page 212, left-hand column, last paragraph).

The difference between claim 1 of the main request and document (16) is the corticosteroid used.

Example 2 of the patent in suit demonstrates, for

several daily doses covering the breadth of claim 1 of the main request, that no or only minimal growth suppression occurs when treatment with ciclesonide is compared with a placebo. There is no reason to assume that these findings are limited to children aged 6 to 12 years. Document (18) provides data comparing ciclesonide with fluticasone propionate. While fluticasone propionate treatment leads to a significantly reduced lower-leg growth rate, treatment with ciclesonide shows growth rates comparable with the placebo (abstract, Figure 1). Document (17) compares ciclesonide with budesonide. Ciclesonide treatment shows a significantly lower reduction in body height than budesonide treatment (abstract, page 396, right-hand column). An effect of reduced growth suppression can thus be acknowledged.

- 7.3 The technical problem is the provision of a safer treatment for asthma in children.

As can be seen from example 2 and the comparative data in documents (17) and (18), the problem has been solved. The issue of whether the growth suppression occurs merely within the time frame of a couple of months or leads to an overall expectation of reduced final body height is not considered to be crucial. Even if the growth suppression could be "made up" at a later stage in a child's development, it still constitutes a major side effect of the treatment.

- 7.4 Document (1) is a publication dedicated to ciclesonide. It generally mentions several side effects of inhaled glucocorticosteroids, such as hypothalamic-pituitary-adrenal (HPA) axis suppression, osteoporosis and juvenile growth retardation (page 80, right-hand column, paragraph 4). Dosage regimens in which such

side effects occur are discussed for beclomethasone and budesonide. There is, however, no such discussion for ciclesonide, despite this glucocorticosteroid being the focus of document (1). In particular, there is no discussion of the side effects of ciclesonide when administered to children. Indeed, document (1) does not mention treating children with ciclesonide. Although document (1) stresses that the intention behind the development of ciclesonide is the provision of good clinical efficacy in asthma treatment while minimising side effects (see page 78, right hand-column, first full paragraph, page 80, right-hand column, fifth paragraph, and page 81, right-hand column, last paragraph), it cannot provide the skilled person with any teaching that ciclesonide could minimise a particular side effect in a patient group not discussed in the document.

Document (14) states that ciclesonide has essentially no oral bioavailability (page 2160, left-hand column, second paragraph) and comes to the conclusion that treatment of healthy volunteers has no clinically relevant systemic effects on the HPA axis (page 2163, left-hand column, last paragraph). The healthy volunteers are adult males (abstract).

In sum, documents (1) and (14) teach that, due to its low oral bioavailability, ciclesonide has reduced side effects in adults. However, these documents provide no pointer that treating children with ciclesonide would be associated with reduced growth suppression compared with established therapies using other inhaled glucocorticoids.

7.5 *Further arguments*

7.5.1 Appellant 2 further argued that it was common ground that inhaled corticosteroids were the most effective therapy available for maintenance treatment of childhood asthma and that the fear of reduced growth velocity was based on exceptional cases and not on group data. Consequently, a skilled person would not have withheld the highly effective treatment with ciclesonide in children with asthma. Furthermore, appellant 2 pointed to the statement in document (21) that doses of 100 to 200 µg of inhaled glucocorticoids were safe (page 531, left-hand column, third paragraph).

As already discussed under point 7.4, the documents relating to ciclesonide do not lead the skilled person to expect reduced growth suppression in children receiving treatment with inhaled corticosteroids. Consequently, whereas a skilled person could have administered ciclesonide to children, they would not have done so in the expectation of reduced growth suppression. The statement of document (21) is not relevant since document (21) does not relate to ciclesonide. It discusses beclomethasone dipropionate, budesonide and fluticasone propionate, but these corticosteroids are used in different daily doses from ciclesonide (see document (16), Table 1; document (17), abstract; document (18), abstract).

7.5.2 Furthermore, appellant 2 considered document (1) to represent an alternative closest prior art. However, appellant 2 has not indicated why document (1) would be more appropriate as closest prior art (see communication pursuant to Article 15(1) RPBA 2007 dated 3 December 2019, point 8.3)

The board does not consider document (1) to represent

the closest prior art. As discussed under point 7.4 above, document (1) is completely silent on treating children with ciclesonide and thus does not represent a promising springboard nor a clear pointer to the solution of the claimed subject-matter

7.6 The subject-matter of claim 1 of the main request involves an inventive step.

8. Documents (28) to (40), submitted by appellant 2 with its statement setting out the grounds of appeal, are not relevant for the outcome of the present decision. Thus, the board does not have to decide on their admission.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the opposition division with the order to maintain the patent with the following claims and a description to be adapted thereto:

claims 1 to 18 of the main request, filed at the oral proceedings of 20 February 2020.

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated