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Datasheet for the decision of 17 October 2023

Case Number: T 1328/21 - 3.3.07

Application Number: 13742573.2

Publication Number: 2874630

IPC: A61K31/519, A61P17/04, A61P37/00

Language of the proceedings: EN

Title of invention:
DOSING REGIMEN FOR JANUS KINASE (JAK) INHIBITORS

Patent Proprietor:
Zoetis Services LLC

Opponent:
KRKA, d.d., Novo mesto

Headword:
DOSING REGIMEN FOR JANUS KINASE (JAK) INHIBITORS/Zoetis Services LLC

Relevant legal provisions:
RPBA 2020 Art. 13(2)
EPC Art. 56

Keyword:
Admission of a document (No)
Main request - Inventive step (No)
Admission of auxiliary request 1 filed during oral proceedings (No)

Decisions cited:

Catchword:

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Case Number: T 1328/21 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 17 October 2023

Appellant: (Opponent)	KRKA, d.d., Novo mesto Smarjeska cesta 6 8501 Novo Mesto (SI)
Representative:	Kutzenberger Wolff & Partner Waidmarkt 11 50676 Köln (DE)
Respondent: (Patent Proprietor)	Zoetis Services LLC 10 Sylvan Way Parsippany, NJ 07054 (US)
Representative:	Mannion, Sally Kim Zoetis UK Limited First Floor, Birchwood Building Springfield Drive Leatherhead, Surrey KT22 7LP (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 16 June 2021 rejecting the opposition filed against European patent No. 2874630 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	E. Duval
Members:	D. Boulois
	S. Ruhwinkel

Summary of Facts and Submissions

I. European patent No. 2 874 630 was granted on the basis of a set of 3 claims.

Independent claim 1 as granted read as follows:

"1. N-methyl-1-{trans-4-[methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino] cyclohexyl}methanesulfonamide, or a pharmaceutically acceptable salt thereof, for use in treating allergic dermatitis, atopic dermatitis, or one or more symptoms thereof selected from pruritus, itch, and skin lesions in a dog in need, wherein a first dose of 0.4 to 0.6 mg/kg body weight is administered to the dog twice a day for a period of from 1 to 14 days followed thereafter by a once a day dose of 0.4 to 0.6 mg/kg body weight".

II. An opposition was filed under Article 100 (a) and (c) EPC against the granted patent on the grounds that its subject-matter lacked novelty and inventive step and extended beyond the content of the application as filed.

III. The present appeal lies from the decision of the opposition division to reject the opposition.

IV. The documents cited during the opposition proceedings included the following:

D1: WO 2010/020905 A1;
D3: Abstracts of the North American Veterinary Dermatology Forum, April 17-20th 20123, Louisville, Kentucky, USA; Vert. Dermatol. 2013: 295-309;

D4: S. Cosgrove et al., Vet. Dermatol., 2013, Dec.; 24(6); 587-597;
D5: Th. Olivry et al., Vet. Dermatol., 2010, Jun.; 21(3):233-248;
D6: Kirk's Current Veterinary Therapy XIV, Saunders Elsevier, 2009, pp 386-388;
D8b: Veterinary Dermatology, 2012, 23(Suppl. 1), 2-104, first page and page 38 containing abstracts FC-35, S. Cosgrove et al., FC-36, T. Fleck et al., and FC-37, D.H. Wheeler at al.;
D11: USA Approved Label for Apoquel;
D15: Declaration by Tina Kotnik;
D15a: Exhibit A - curriculum vitae of Tina Kotnik;
D15b: Exhibit B - Th. Olivry et al., Veterinary Dermatology 2010, 21, 4-22; citation [16] of D5;
D15c: Exhibit C - J. Ring et al., JEADV 2012, 26, 1176-1193 D15d: Evidence on publication date of Exhibit C;
D16: Second declaration of Dawn M. Claever, DVM;

V. According to the decision under appeal, the claims of the patent as granted fulfilled the requirements of Article 123(2) EPC and were novel over D3.

With regard to inventive step, D1 was the closest prior art; Example 6 of D1 disclosed the treatment of dogs with flea-associated pruritus and dermatitis with the closest dosing regimen being 0.5 mg/kg oclacitinib maleate, i.e. the claimed comöound, given twice a day for 28 days. The claimed dosage regimen differed in the presence of a second period of administration of only once a day, instead of administering the compound continuously twice a day. The problem to be solved was formulated as the provision of an alternative treatment regimen for the same dogs of D1 which has improved

safety for long term administration. The claimed solution was not obvious in view of D1, D5 and D6.

VI. The opponent (hereinafter the appellant) filed an appeal against said decision.

VII. With its reply to the statement of grounds of appeal dated 15 March 2022, the patent proprietor (hereinafter the respondent) filed auxiliary requests 1-8 and 3b, 4b.

VIII. A communication from the Board, dated 21 June 2023, was sent to the parties. In this, it was stated in particular that, with regard to inventive step, the technical problem to be solved over the closest prior art D1 was the provision of an alternative administration regimen and that obviousness would be debated during oral proceedings.

IX. With a letter dated 6 September 2023, the respondent submitted the following item of evidence:

D17: EMA Summary of Product Characteristics (SmPc) for Apoquel

X. Oral proceedings took place on 17 October 2023. During the oral proceedings the respondent withdrew auxiliary requests 1-8, 3b and 4b filed with letter of 15 March 2022 and filed a new auxiliary request 1.

In comparison to claim 1 of the main request (corresponding to the patent as granted), claim 1 of auxiliary request 1 has been amended by the following supplementary feature "wherein the treatment is for chronic use."

XI. The arguments of the appellant may be summarised as follows:

Admission of D17 into the appeal proceedings

This document should not be admitted, since it could have been filed earlier during the opposition proceedings.

Main request - Inventive step

The closest prior art was D1, in view of example 6, and the distinguishing feature was the dose regimen; Figures 2 and 3 of D1 showed that the treatment was efficient. There was no technical effect demonstrated, in particular in view of Tables 4, 5 and paragraph [0045] of the contested patent, which showed that the dose regimen of D1 was safe. The interpretation of the data of Figure 1 of the contested patent was a simple allegation not demonstrated by experimental evidence; it could be relevant after a long period, but not for shorter duration of administration as claimed. Claim 1 of the main request did not require a total period of treatment, which could be a minimum of two days, the claimed subject-matter covered also a very short term treatment. The problem was the provision of an alternative dose regimen and the solution was obvious in view of D1, which suggested a single daily dose.

Admission of auxiliary request 1 into the appeal proceedings

There were no exceptional circumstances justifying the filing of a new request during oral proceedings. This request should and could have been filed earlier in response to the appeal. Moreover, all objections

regarding the duration of treatment were already present in the statement of grounds o appeal. Finally the amendment was not limited to a long term treatment, was unclear and was not relevant.

XII. The arguments of the respondent may be summarised as follows

Admission of D17 into the appeal proceedings

This document should be admitted in the proceedings, even if it was not essential. It provided the same evidence than D11.

Main request - Inventive step

The purpose of the claimed invention was the treatment of chronic conditions, in particular a lifetime treatment (cf. D15a) and not a short term treatment of two days as argued by the appellant. There were two distinguishing features over D1 and the effects were an improved efficacy and safety for a long-term administration. D1 did in particular not address the problem of safety linked with a possible chronic immunosuppression, which was illustrated by Figure 1 of the patent. The safety of the treatment was also confirmed by D11. There was no suggestion for modifying the dose regimen disclosed in D1, and the claimed solution was obvious for this reason.

Admission of auxiliary request 1 into the appeal proceedings

The amendment brought to claim 1 was simple and was a response to the decision of the Board with regard to inventive step, since no improvement was shown on a

short time, and it was a further distinguishing feature over D1. It was the first time that this argument was brought during the proceedings, and it was not clear that the interpretation of the claim was linked with the absence of a claimed time period. The feature was able to overcome the inventive step objection and was clear, meaning that the treatment was for a long-time, in particular for a lifetime.

XIII. Requests

The appellant requested that the decision under appeal be set aside and that the patent be revoked. The appellant also requested that document D17, filed by the respondent with their letter from 6 September 2023, not be admitted into the proceedings.

The respondent requested that the appeal be dismissed, alternatively that the decision under appeal be set aside and the patent be maintained according to the set of claims filed as auxiliary request during the oral proceedings before the Board on 17 October 2023.

Reasons for the Decision

1. Admission of D17 into the appeal proceedings

1.1 D17 was filed by the respondent with its letter dated 6 September 2023 and is an EMA summary of the product characteristics (SmPc) of Apoquel comprising the claimed active agent oclacitinib. This document was cited by the respondent in the framework of the assessment of inventive step; the respondent relied indeed *inter alia* on D11 and D17 to confirm the technical effects announced in the application as

filed. The respondent mentioned furthermore during the oral proceedings that D17 provided the same evidence than D11.

1.2 Article 13(2) RPBA 2020 is relevant for the assessment of the admission of D17. According to Article 13(2) RPBA 2020, any amendment to a party's case after notification of a summons to oral proceedings shall, in principle not be taken into account, unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

In the present case, there are no exceptional circumstances which have been justified by the respondent for the submission of D17. The Board did in particular not raise any new point or argument in its preliminary opinion in the context of the discussion of the assessment of inventive step. Moreover, the information given in D17 appears to be redundant with the information provided by other documents already on file, as confirmed by the respondent in view of D11.

Consequently, the Board decides to not admit D17 into the appeal proceedings (Article 13(2) RPBA 2020).

2. Main request - Inventive step

2.1 The invention relates to the compound N-methyl-1-{trans-4-[methyl(7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]cyclohexyl}methanesulfonamide, also known as oclacitinib, for use in treating allergic dermatitis, atopic dermatitis, or one or more symptoms thereof selected from pruritus, itch, and skin lesions in a dog. The invention aims in particular to maintain an inhibition corridor in a dog comprising administering oclacitinib according to a specific dosage regimen, in

order to reach the inhibition of interleukin associated with a target disease state while minimizing modulation of other cytokines associated with toxicity. This allows the maximization of the positive drug effects while minimizing or eliminating the side effects (see par. [0010] and [0012]).

2.2 The closest prior art is D1. Example 6 of D1 discloses the treatment of dogs with flea-associated pruritus and dermatitis with the dose regimen being 0.5 mg/kg oclacitinib maleate given twice a day (BID) for 28 days. Figures 2 and 3 of D1 show explicitly the reduction on the lesions and erythema, as well as on pruritus associated with the dose of 0.5 mg/kg.

FIGURE 2

VAS Scores for Example 1b in flea allergic dogs

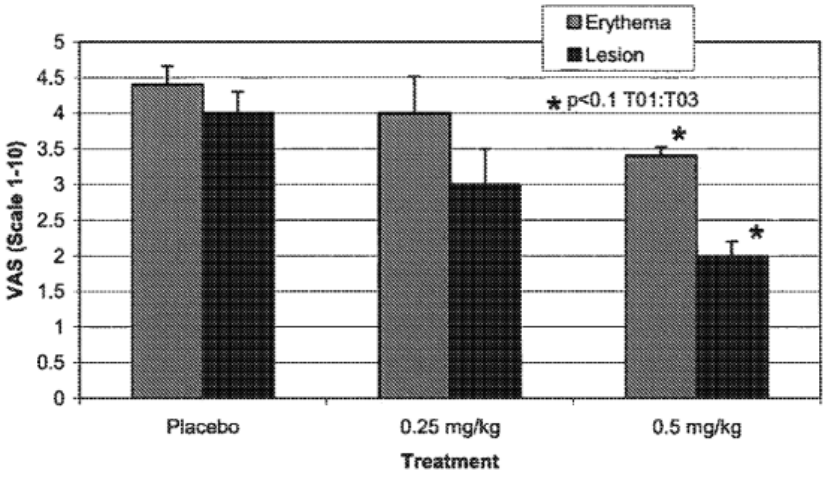
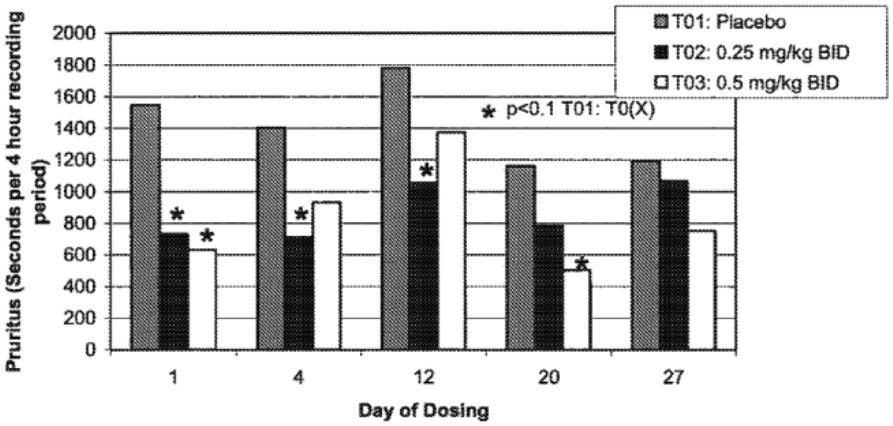


FIGURE 3

Seconds of Pruritus per 4 hour recording for Example 1b in flea allergic dogs



D1 suggests different dosages of the active compound in a range from 0.01 to 100 mg/kg, preferably from 0.3 to 1.5 mg/kg in a single dose or multiple doses (see par. [0042]-[0043]).

This document does not disclose a second period of administration only once a day (SID) after 14 days instead of administering the compound continuously twice a day (BID). This feature constitutes the distinguishing feature between the claimed subject-matter and the disclosure of D1.

The Board does in particular not agree with the respondent that the technical distinguishing features between the claimed subject-matter and the disclosure of D1 were two in number, namely a first higher dose of 0.4 to 0.6 mg/kg body weight administered to the dog twice a day for a period of from 1 to 14 days and not 28 days as in claim 1, and a second once a day dose of 0.4 to 0.6 mg/kg body weight instead of twice a day. In the Board's view, the dosage regimen must indeed be considered as a whole and cannot be separated in several distinct phases. The difference is therefore

the dosage regimen and simply lies in the fact that the administration twice a day changes to once a day after a certain number of days, i.e 1 to 14 days, within the total 28 days of treatment as disclosed in D1.

2.3 The opposition division defined the problem as the provision of a treatment regimen for the same dogs of D1 which has improved safety for long term administration.

The respondent defines the problem to be solved as the provision of an improved efficacious treatment regimen for dogs, which has improved safety for long-term administration.

The appellant disagrees with these definitions, and sees the problem as the provision of an alternative administration regimen, i.e. without the requirement of being efficacious and without the requirement of providing improved safety.

2.4 The solution to any of these problems is oclacitinib or a pharmaceutically acceptable salt thereof, for use in treating allergic dermatitis, atopic dermatitis, or one or more symptoms thereof selected from pruritus, itch, and skin lesions in a dog in need, wherein oclacitinib is administered in a first dose of 0.4 to 0.6 mg/kg body weight to the dog twice a day for a period of from 1 to 14 days followed thereafter in particular by a once a day dose of 0.4 to 0.6 mg/kg body weight.

2.5 The parties cited the contested patent and documents D4, D11 and D8b in support of the achievement of a technical effect and the definition of the problem.

2.6 The contested patent

2.6.1 Several studies were performed in the examples of the contested patent:

(a) Table 2 shows the effect on pruritus by the administration of 0.4-0.6 mg/kg BID (twice per day) of oclacitinib for 7 days. The VAS score is an improved score of 25 mm, while the placebo was at 55 mm. Table 3 shows again the effect on pruritus by the administration of 0.4-0.6 mg/kg BID of oclacitinib for 14 days, obtaining an improved VAS score of 18 mm. These studies confirm the efficacy of oclacitinib at 0.4-0.6 mg/kg BID given for 7 or 14 days.

(b) Table 4 and 5 are long term studies on the administration of 0.4-0.6 mg/kg BID of oclacitinib during 112 and 84 days. The dose regimen showed excellent efficacy for the control of atopic dermatitis including pruritus and was safe for up to 90 to 112 days of treatment of dogs (see paragraph [0040]). The same passage in paragraph [0040] mentions that the same regimen was safe for up to 90 days at elevated dosages, without further specification of the dosage it refers to.

(c) A dose selection study was shown in Table 6 over 112 days. The VAS scores for atopic dermatitis over the 112 days of study were in the following order from highest VAS score (highest demonstration of atopic dermatitis) to lowest VAS score: T01, T04, T03 and T02. The CADESI score were in the same following order from the highest (highest demonstration of atopic dermatitis) to the lowest: T01 (placebo), T04 (0.2-0.3 mg/kg SID oclacitinib), T03 (0.4-0.6 mg/kg SID oclacitinib), and T02 (0.4-0.6 mg/kg BID for 14 days followed by 0.4-0.6

mg/kg SID thereafter which is as claimed in claim 1 of the main request).

(d) An animal safety study was shown in paragraph [0045] in the form of a comparison between doses of 0.0 mg/kg, 0.6 mg/kg, 1.8 mg/kg and 3.0 mg/kg of oclacitinib, twice per day during weeks 1-6 and then once per day during weeks 7-26. The treatment was well tolerated at all dose multiples (par. [0046]).

2.6.2 None of these studies provides a comparison between a dose regimen as claimed of 0.4-0.6 mg/kg BID during 1 to 14 days and 0.4-0.6 mg/kg SID thereafter, and the dose regimen disclosed in D1, namely 0.5 mg/kg BID during 28 days, and these studies are therefore not conclusive to show any advantage linked with the claimed dose regimen over the dose regimen disclosed in D1.

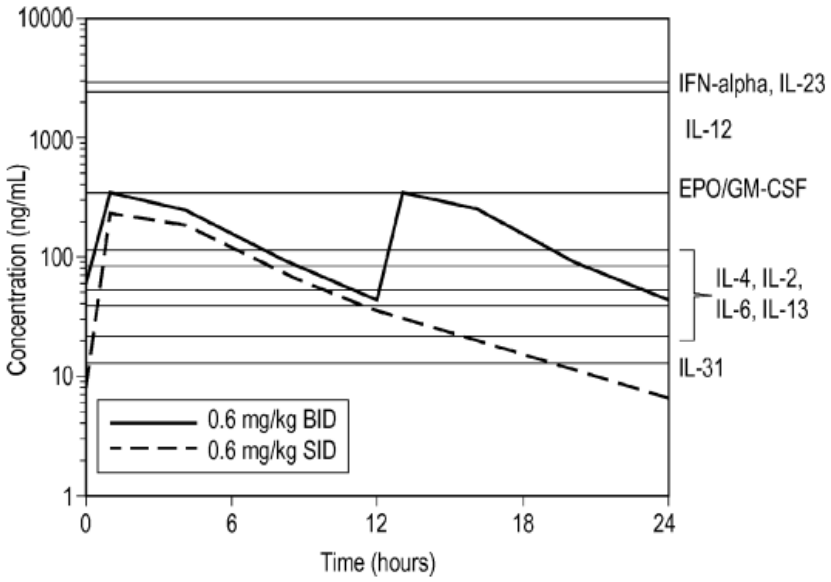
2.6.3 Several data, such as in Tables 2-5, show furthermore that a dose regimen of 0.4-0.6 mg/kg BID showed excellent efficacy for the control of atopic dermatitis including pruritus, which confirms the data on the efficacy of this dose regimen provided by D1, in particular in its Figures 2 and 3.

2.6.4 More significantly, the data of Tables 4 and 5 and of paragraph [0045] of the contested patent explicitly underline that a dose regimen of 0.4-0.6 mg/kg BID administered during respectively 112 and 84 days, as well as of 0.6 mg/kg BID administered during 6 weeks, were safe and well tolerated. This appears to be a clear and explicit evidence that the dose regimen disclosed in D1 is safe and that the dose regimen as claimed does not provide an improved safety for long-term administration over the dose regimen disclosed in

D1 for a duration of 28 days, and even as long as of 112 days.

2.6.5 The Board could in particular not follow the argumentation of the respondent that the dose regimen disclosed in D1 would result in a chronic immunosuppression and leads to increased side effects of the infectious type, through the maintenance of a dose of 0.5 mg/kg BID during 28 days. This argument is based on the existence of an inhibition corridor linked with the claimed dose regimen, in particular with the maintenance dose of 0.4-0.6 mg/kg SID after 1-14 days, as illustrated by Figure 1 of the contested patent:

Figure 1



According to Figure 1 and the corresponding explanations in paragraphs [0010] and [0012] of the contested patent, the claimed dose regimen achieves an inhibition corridor between efficacy-related cytokines

(IL-4, IL-2, IL-6 or IL-13 in Figure 1) and toxicity related cytokines (IFN-alpha, I-23, IL-12 in Figure 1), therefore achieving a highly efficacious treatment while also minimizing or eliminating side-effects. The absence of relief in the inhibition the efficacy-related cytokines (IL-4, IL-2, IL-6 or IL-13 in Figure 1) seen with the constant administration of 0.4-0.6 mg/kg BID results however in a possible chronic immunosuppression, which leaves the dogs more susceptible to infections, which can be avoided by the switch to the claimed maintenance dose of 0.6 mg/kg SID applied after 1-14 days. The dotted curve in Figure 1 shows therefore a daily interruption of the inhibition of the toxicity-related cytokines which allows the levels of oclatinib to fall below the IC50s for IL-2, IL-4, IL-6 and IL-13 and provides a relief in which these cytokines recover and are able to contribute to the normal functioning of the immune system.

In the Board's view, the relief of the chronic immunosuppression shown in Figure 1 is only shown theoretically and is not supported by any experimental evidence. It is indeed not demonstrated that such an inhibition corridor and in particular the absence of chronic immunosuppression is not observed with the dose regimen disclosed in D1, namely 0.5 mg/kg BID during 28 days. In other words, Figure 1 does not provide any proof that a dose regimen of 0.4-0.6 mg/kg BID as disclosed in D1 involves a chronic immunosuppression and the emergence of side effects, in particular of the infectious type.

Moreover, this argument is clearly and explicitly refuted by the experiments shown in the contested patent. The absence of any side effects of the infection type is indeed confirmed in view of the

safety results obtained with a dose regimen of 0.4-0.6 mg/kg BID, as shown in Tables 4 and 5 and of paragraph [0045] during a much longer period than 28 days, as long as 112 days. The patent gives rather indications that only higher doses or long term administration may be responsible of such chronic immunosuppression (see also par. [0047]). The contested patent mentions for instance that a high dose of 3 mg/kg BID given during 6 months to dogs showed side effects, such as in particular bacterial and parasitical pneumonia. Hence, the safety of the dose regimen of D1 is directly and unambiguously demonstrated by the data of the contested patent.

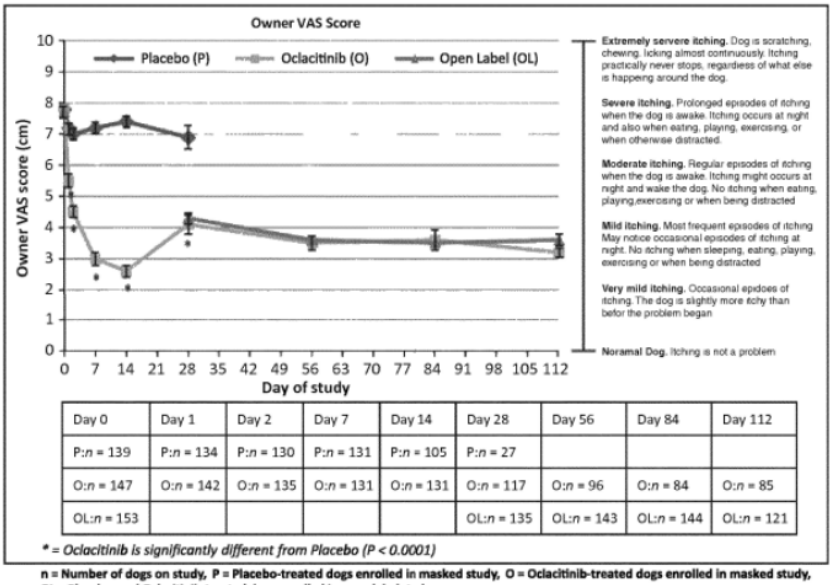
Finally, as also argued by the appellant, Figure 1 is a 24 hour representation of the effect of oclacitinib, without any indication of time scale wherein this daily representation might take place, after 14 days, 28 days or 150 days; for this reason the effect shown in Figure 1 cannot be taken in account. It cannot be excluded that the theoretical effect shown in Figure 1 might be relevant after a prolonged period of administration, but this cannot be taken in account, since a prolonged period of time is not claimed. The subject-matter of claim 1 is indeed not restricted to a long-term treatment and includes a duration of treatment as short as the 28-day treatment of D1, namely up to 14 days at 0.4-0.6 mg/kg BID followed by the remaining days at 0.4-0.6 mg/kg SID. Accordingly, the possibility of a chronic immunosuppression after 28 days is neither credible nor supported by Figure 1 and this effect cannot be taken in account in view of the claimed subject-matter.

2.6.6 In conclusion and in view of the experiments disclosed in the contested patent, it is not possible to conclude

that the claimed dose regimen presents a technical effect or an advantage over the dose regimen disclosed in D1, even with regard to the safety of the treatment.

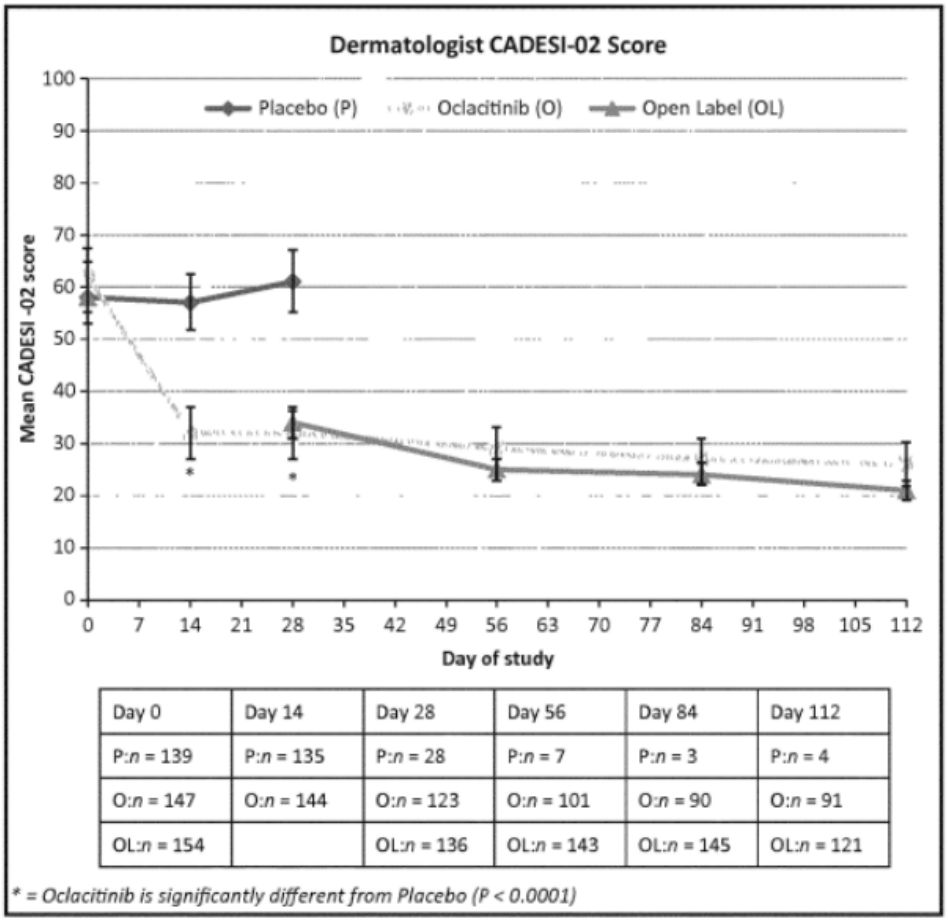
2.7 Document D4

D4 shows a comparison between the administration of oclacitinib at 0.4-0.6 mg/kg BID for 14 days and then SID for up to 112 days, versus an open label study administering oclacitinib at 0.4-0.6 mg/kg SID during 112 days. The results on pruritus according to VAS score and CADESI-02 score are shown below in Figures 1 and 2:



Day 0	Day 1	Day 2	Day 7	Day 14	Day 28	Day 56	Day 84	Day 112
P:*n* = 139	P:*n* = 134	P:*n* = 130	P:*n* = 131	P:*n* = 105	P:*n* = 27			
O:*n* = 147	O:*n* = 142	O:*n* = 135	O:*n* = 131	O:*n* = 131	O:*n* = 117	O:*n* = 96	O:*n* = 84	O:*n* = 85
OL:*n* = 153					OL:*n* = 135	OL:*n* = 143	OL:*n* = 144	OL:*n* = 121

Figure 1. Owner Pruritus visual analog scale (VAS) scores by day of study (95% confidence interval).



Day 0	Day 14	Day 28	Day 56	Day 84	Day 112
P:*n* = 139	P:*n* = 135	P:*n* = 28	P:*n* = 7	P:*n* = 3	P:*n* = 4
O:*n* = 147	O:*n* = 144	O:*n* = 123	O:*n* = 101	O:*n* = 90	O:*n* = 91
OL:*n* = 154		OL:*n* = 136	OL:*n* = 143	OL:*n* = 145	OL:*n* = 121

n = Number of dogs on study, P = Placebo-treated dogs enrolled in masked study, O = Oclacitinib-treated dogs enrolled in masked study, OL = Placebo- and Oclacitinib-treated dogs enrolled in open-label-study

It appears difficult to draw any conclusion with regard to the disclosure of D4, apart from the efficacy of the claimed dose regimen, and that a BID/SID treatment appears to provide a comparable efficacy over a SID treatment over 112 days. There is however no comparison made with the disclosure of D1.

2.8 Document D11

D11 is the FDA approved label of Apoquel, a tablet of oclacitinib. The administration dose of Apoquel (oclacitinib) is 0.18 to 0.27 mg oclacitin/lbs (0.4 to 0.6 mg/kg) body weight, administered orally, twice daily for up to 14 days, and then administered once

daily for maintenance therapy. D11 confirms the efficiency of this dose regimen.

D11 provides also an animal margin safety study (see "Animal Safety" on the second page), which is a safety study performed in exaggerated situations, and wherein oclacitinib was administered to healthy 12 months old dogs twice daily for 6 weeks, followed by once daily for 20 weeks, at 0.6 mg/kg, 1.8 mg/kg and 3.0 mg/kg. D11 mentions that the dose regimens used have as effect a mild, dose-dependent reduction in hemoglobin, hematocrit, and reticulocyte counts during the twice daily dosing period with decreases in the leukocyte subsets of lymphocytes, eosinophils, and basophils. A second safety study in 6-month-old dogs was however discontinued after four months due to the development of bacterial pneumonia and generalized demodex mange infections in dogs in the high dose (3X and 5X) treatment groups, i.e at 1.8 and 3.0 mg/kg oclacitinib twice daily, for the entire study.

Hence, D11 mentions indeed an impact on some biological levels linked with a dose regimen of 0.6 mg/kg BID during 6 weeks, but this is not translated into safety problems or serious side effects for the dogs. Such infectious safety problems are only mentioned with dose regimens of 1.8 and 3.0 mg/kg BID oclacitinib.

Consequently, D11 confirms in fact that a dose of 0.4-0.6 mg/kg BID during a period as long as 6 weeks does not have any impact on safety and that the dose regimen disclosed in D1, namely 0.5 mg/kg BID during 28 days is safe. In view of D11, as for the experiments disclosed in the contested patent, it is not possible to conclude that the claimed dose regimen presents a technical effect or an advantage over the dose regimen

disclosed in D1, in particular with regard to the safety of the treatment.

2.9 Document D8b

This document relates to the treatment of 0.4 mg/kg oclacitinib twice daily for 14 days, and shows the efficiency of the treatment on pruritus and also its safety. Hence, this document does not provide any comparison with the dose regimen of D1 and cannot be considered as relevant.

2.10 Consequently, none of the cited documents appear to show a technical effect linked with the distinguishing feature, i.e. the once a day dose of oclacitinib after a first period of 1-14 days with a twice daily administration. More particularly, the teaching of the patent or as shown in D11 does not appear to show any improvement with regard to efficacy or to the appearance of side effects in comparison with the dose regimen as disclosed in D1.

Accordingly, the problem is as defined by the appellant, namely the provision of an alternative administration regimen.

2.11 Obviousness of the solution

Since the problem consists in the provision of an alternative dose regimen, it would be sufficient that there is a pointer in the prior art for the claimed solution, or that said solution results from the knowledge and competence a skilled person must be assumed to have, such as a routine or standard modification to conclude to a lack of inventive step.

In the present case, D1 suggests to use a preferable dose of 0.3 to 1.5 mg/kg of body weight per day, which could be spread in a single dose or in divided doses (see D1, par. [0042]-[0043]). The maintenance dose of 0.4-0-6 mg/kg SID falls within the daily dose range that is envisaged and considered therapeutically effective in D1. For this reason alone, the claimed solution appears to be an arbitrary choice and is not inventive over D1.

Moreover, as pointed out by the appellant, there is no prejudice in view of the teaching of D1 to use a lower dose for a good level of efficacy. Figure 3 of D1 shows indeed that for a dose of 0.25 mg/kg BID, which is a dose close to the claimed dose of 0.5 mg/kg SID, the values for pruritus is not substantially lower than for a dose of 0.5 mg/kg BID.

Consequently, the claimed subject-matter lacks inventive step over D1 and the main request does not meet the requirements of Article 56 EPC.

3. Admission of auxiliary request 1 into the appeal proceedings

3.1 This request has been filed during the oral proceedings after the Board announced its conclusion on the main request. In comparison to claim 1 of the main request, the feature "**wherein the treatment is for chronic use**" has been added, and this feature is an amendment originating from the description. According to the respondent, this request was filed during oral proceedings since the Board indicated for the first time that this conclusion was linked with the interpretation of the claim and the absence of any claimed time period. This point would in particular not

have been expressed in the preliminary opinion of the Board.

3.2 This new request has been filed at a very late stage of the appeal proceedings, during the oral proceedings and after a conclusion on inventive step had been announced on the main request. Article 13(2) RPBA 2020 is relevant (Article 25(3) RPBA 2020) for the assessment of the admission of this new request. According to Article 13(2) RPBA 2020, any amendment to a party's case after notification of a summons to oral proceedings shall, in principle not be taken into account, unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned. Such exceptional circumstances might for instance reside in objections or arguments formulated for the first time in the provisional opinion of the Board or during the oral proceedings before the Board.

This is presently not the case. The appellant mentioned indeed repeatedly in its statement of grounds of appeal that the dose regimen of claim 1 was not limited to any extended duration, and encompassed regimen as short as 2 days, and that the experiments of the patent could not support credibly the existence of an effect, since they all related to a longer period of administration (see statement of grounds of appeal, page 3, point 3.3.2. or page 5 point 3.3.4). This argument was repeated in the second letter of the appellant dated 19 July 2023 (see page 3, point 2.2.3, page 6, 2nd par. or page 7, point 3.2.2).

The Board also mentioned the same point in its communication dated 21 June 2023 by repeating the appellant's arguments (see point 12.4.5 of the

communication). The Board concluded by defining the technical problem as the provision of an alternative administration regimen.

This argument cannot therefore constitute a surprise to the respondent and there are no exceptional circumstances justifying the filing of a new request at this stage of the appeal proceedings. Moreover, it is questionable whether the feature **"wherein the treatment is for chronic use"** answers this specific argumentation raised by the appellant with regard to the assessment to inventive step and whether it meets the requirements of clarity. This adds complexity to the case.

Consequently, the Board decides to not admit auxiliary request 1 into the appeal proceedings (Article 13(2) RPBA 2020).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked

The Registrar: The Chairman:

B. Atienza Vivancos E. Duval

Decision electronically authenticated