Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 28 November 2023

Case Number: T 0056/22 - 3.3.04

Application Number: 17185704.8

Publication Number: 3260117

IPC: A61K31/135, A61K9/28, A61K9/20, A61P5/18

Language of the proceedings: EN

Title of invention:
Rapid dissolution formulation comprising cinacalcet HCl

Patent Proprietor:
Amgen Inc.

Opponents:
Glenmark Pharmaceuticals Europe Ltd
BIOGARAN
HGF Limited
Aechter, Bernd
betapharm Arzneimittel GmbH
TAD Pharma GmbH
PUREN Pharma GmbH & Co. KG

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - (no)

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 0056/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 28 November 2023

Appellant: (Patent Proprietor)	Amgen Inc. One Amgen Center Drive Thousand Oaks, CA 91320-1799 (US)
Representative:	Uexküll & Stolberg Partnerschaft von Patent- und Rechtsanwälten mbB Beselerstraße 4 22607 Hamburg (DE)
Appellant: (Opponent 2)	Glenmark Pharmaceuticals Europe Ltd Building 2, 1st Floor Croxley Green Business Park Watford Hertfordshire WD18 8YA (GB)
Representative:	Schlich, George Schlich 9 St Catherine's Road Littlehampton, West Sussex BN17 5HS (GB)
Appellant: (Opponent 4)	BIOGARAN 15 Boulevard Charles de Gaulle 92707 COLOMBES (FR)
Representative:	Casalonga 31 Rue de Fleurus 75006 Paris (FR)
Appellant: (Opponent 6)	Aechter, Bernd Ter Meer Steinmeister & Partner Patentanwälte mbB Nymphenburger Straße 4 80335 München (DE)
Representative:	Ter Meer Steinmeister & Partner Patentanwälte mbB

Nymphenburger Straße 4
80335 München (DE)

Appellant: (Opponent 7)
betapharm Arzneimittel GmbH
Kobelweg 95
86156 Augsburg (DE)

Representative:
Hamm&Wittkopp Patentanwälte PartmbB
Jungfernstieg 38
20354 Hamburg (DE)

Appellant: (Opponent 8)
TAD Pharma GmbH
Heinz-Lohmann-Straße 5
27472 Cuxhaven (DE)

Representative:
Hoefer & Partner Patentanwälte mbB
Pilgersheimer Straße 20
81543 München (DE)

Appellant: (Opponent 10)
PUREN Pharma GmbH & Co. KG
Willy-Brandt-Allee 2
81829 Munich (DE)

Representative:
Hamm&Wittkopp Patentanwälte PartmbB
Jungfernstieg 38
20354 Hamburg (DE)

Respondent: (Opponent 5)
HGF Limited
1 City Walk
Leeds Yorkshire LS11 9DX (GB)

Representative:
HGF
HGF Limited
1 City Walk
Leeds LS11 9DX (GB)

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 12 November 2021 concerning maintenance of the European Patent No. 3260117 in amended form.**

Composition of the Board:

Chairwoman M. Pregetter
Members: R. Hauss
L. Bühler
A. Chakravarty
M. Blasi

Summary of Facts and Submissions

I. European patent No. 3 260 117 (patent in suit) was granted with a set of 12 claims. Claim 1 reads as follows:

1. A pharmaceutical composition comprising

a) from 5% to 40% by weight of cinacalcet HCl;

b) a pharmaceutically acceptable excipient comprising microcrystalline cellulose and starch in a weight ratio ranging from 1:1 – 15:1;

wherein at least one dosage unit of the pharmaceutical composition has a dissolution profile in 0.05 N HCl, measured according to a dissolution test conducted in a USP 2 apparatus at a temperature of 37°C ± 0.5°C, and at a rotation speed of 75 r.p.m., which comprises from 50% to 125% of a target amount of the cinacalcet being released from the composition no later than about 30 minutes from the start of the test.

II. Six oppositions were filed against the patent in suit. After the expiry of the opposition period, four interventions to the proceedings before the opposition division occurred (Article 105 EPC).

The patent in suit 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 both the application as filed (No. EP 17 185 704.8) and the earliest parent application as filed.

III. Before the opposition division, the patent proprietor requested that the patent in suit be maintained as granted, i.e. that the oppositions be rejected. It also submitted amended sets of claims as auxiliary requests 1 to 9.

IV. Opponent 3 withdrew its opposition. After the oral proceedings before the opposition division, opponent 1 also withdrew its opposition.

V. The documents cited in the proceedings before the opposition division included the following:

D1: Expert Opin. Investig. Drugs 12(8), 1413-1421 (August 2003)

D4a: Lieberman et al. (editors), Pharmaceutical Dosage Forms: Tablets, vol. 1, 2nd edn. 1989, Chapters 3-4

D10: A. Wade, P.J. Weller (editors), Handbook of Pharmaceutical Excipients, 2nd edn. 1994, 482-493

D10a: A. Wade, P.J. Weller (editors), Handbook of Pharmaceutical Excipients, 2nd edn. 1994, 84-87, 143-144, 491-493

D14: J. Am. Soc. Nephrol. 14, 575-583 (2003)

D75: The AAPS Journal 21, article no. 32 (2019)

D152: Experimental report No. 3 (filed by opponent 8)

VI. The decision under appeal is the opposition division's interlocutory decision, announced on 6 July 2021 and handed over to the postal service provider on 12 November 2021. In this decision, the opposition division found the intervention by opponent 9 inadmissible. It also found that the ground for opposition under Article 100(c) EPC prejudiced the maintenance of the patent as granted and that the

patent as amended in the form of auxiliary request 1 met the requirements of the EPC.

The claims of this request differ from those of the patent as granted (main request) in that several dependent claims have been deleted. Claim 1 of auxiliary request 1 is identical to claim 1 as granted.

VII. The patent proprietor and opponents 2, 4, 6, 7, 8 and 10 all filed appeals against this decision.

VIII. Opponents 5 and 9 did not file appeals. As opponent 9 did not appeal, the ruling that its intervention in the opposition proceedings was not admissible became final.

IX. With its statement setting out its grounds of appeal dated 21 March 2022, the patent proprietor requested as its ***main request*** that the patent be maintained as granted, implying that the oppositions be rejected, and it also filed a further set of claims as ***auxiliary request 1***. Claim 1 of this new auxiliary request 1 is identical to claim 1 as granted (see section I. above).

X. With its reply to the opponents' grounds of appeal dated 8 August 2022, the patent proprietor submitted auxiliary claim requests 2 to 10. These requests are identical to former auxiliary claim requests 1 to 9 as filed in the proceedings before the opposition division.

Thus, the claims of ***auxiliary request 2*** are identical to those of former auxiliary request 1, which was held allowable in the decision under appeal (see section VI. above). As already mentioned, claim 1 of this request is identical to claim 1 as granted.

Claim 1 of ***auxiliary request 3*** is identical to claim 1 as granted, except that "37 ± 0.5°C" has been replaced by "37°C".

Claim 1 of ***auxiliary request 4*** is identical to claim 1 as granted, except that it further specifies that the composition is in a form chosen from tablets and capsules.

Claim 1 of ***auxiliary request 5*** is identical to claim 1 of auxiliary request 3, except that it further specifies that the composition is in a form chosen from tablets and capsules.

Claim 1 of ***auxiliary request 6*** is identical to claim 1 of auxiliary request 3, except that it specifies that "the composition is a tablet".

Claim 1 of ***auxiliary request 7*** is identical to claim 1 of auxiliary request 5, except that "from 50% to 125%" has been replaced by "from 85% to 125%".

Claim 1 of ***auxiliary request 8*** is identical to claim 1 of auxiliary request 5, except that "from 50% to 125%" has been replaced by "from 85% to 100%".

Claim 1 of ***auxiliary request 9*** is identical to claim 1 of auxiliary request 6, except that "from 50% to 125%" has been replaced by "from 85% to 125%".

Claim 1 of ***auxiliary request 10*** is identical to claim 1 of auxiliary request 6, except that "from 50% to 125%" has been replaced by "from 85% to 100%".

XI. In the course of the appeal proceedings, the parties submitted further documents as evidence. Documents D124 and D153 to D158 were filed by the opponents. Documents D159 and D160 were filed by the patent proprietor.

XII. In response to a summons to oral proceedings, issued by the board in view of corresponding requests by the parties, opponents 5 and 6 indicated they would not be attending.

XIII. Oral proceedings before the board were held on 28 November 2023, in the absence of opponents 5 and 6 (Article 15(3) RPBA and Rule 115(2) EPC). Opponent 6 was considered to rely on his written submissions. Opponent 5 had not presented any written submissions in the appeal proceedings. At the end of the oral proceedings, the board revoked the patent in suit for lack of inventive step.

XIV. The opponents' arguments can be summarised as follows:

The definition of the dissolution profile in claim 1 as granted was unclear, on account of the phrasing "at least one dosage unit of the pharmaceutical composition" and the absence of any definition of the "target amount". Furthermore, it was not the composition as claimed but only one dosage unit thereof (and not another one) that was required to have the specified dissolution profile. As a consequence, the dissolution profile should not be taken into account as a distinguishing feature in the assessment of patentability, specifically of inventive step.

Starting from the disclosure of document D1, the objective technical problem should then be defined as providing an alternative pharmaceutical composition comprising cinacalcet HCl, since no specific technical effect had been demonstrated. In particular, there was no causal technical relationship between the structural features defined under items a) and b) in claim 1, which left almost 95% of the composition undefined, and the technical effect of rapid release alleged by

the patent proprietor. The qualitative and quantitative features defined under items a) and b) of claim 1 would have been obvious choices for a person skilled in the art seeking to provide a further composition of cinacalcet HCl.

If the dissolution profile in claim 1 were to be understood as limiting the claimed compositions to only those providing rapid dissolution (as argued by the patent proprietor), then it would not be correct to define the objective technical problem as providing a composition with rapid dissolution (as suggested by the patent proprietor). This was because the objective technical problem had to be formulated in a way that did not contain any pointer to its solution. Defining the solution to the objective technical problem solely by a desideratum (i.e. in the case at hand the desired dissolution profile) could not be considered an inventive contribution to the art.

If, however, the objective technical problem were to be defined as providing a pharmaceutical composition of cinacalcet HCl with rapid dissolution, preparing a composition with a suitable dissolution profile would have been an obvious measure to solve this problem. The person skilled in the art would have had the knowledge of galenics required to optimise dissolution profiles, as this was a routine activity in galenic formulation that was based on common general knowledge.

The same considerations applied to claim 1 of the auxiliary requests. With regard to claim 1 of auxiliary request 6, which required the composition to be a tablet, it should be taken into account that D1 disclosed favourable pharmacokinetics of cinacalcet HCl. Consequently, no special measures would have been required in formulating cinacalcet HCl as a tablet. The person skilled in the art would have used

standard excipients such as those claimed. It was also part of the skilled person's common general knowledge to formulate compositions so as to present a desired dissolution profile.

XV. The patent proprietor's arguments can be summarised as follows:

It was evident that a pharmaceutical composition could comprise multiple dosage units. The target amount in claim 1 was the average amount or label amount of cinacalcet present in the dosage units. The range given for the proportion of substance released within 30 minutes, i.e. "50% to 125% of a target amount", with an upper limit of more than 100%, had to be understood in the context of known standard requirements for dosage-unit conformity. This parameter was determined by analysing a number of dosage-unit samples, the standard being that no dosage unit should be outside a range of 75% to 125% of the target amount (see paragraph [0044] of the patent in suit).

In light of the description, feature (b) of claim 1 would be understood to require the presence of more than just negligible minor amounts of microcrystalline cellulose and starch. The example formulations described (see paragraph [0057] of the patent in suit) contained substantial proportions (more than 70% by weight) of these compounds together with 18% by weight of cinacalcet HCl. It was thus clear that the components addressed in features (a) and (b) of claim 1 were all major components of the claimed composition.

The patent in suit showed dissolution profiles of the exemplified formulations (paragraph [0069]) according to which at least 75% of the cinacalcet HCl was released within 30 minutes. On this basis, it should be accepted that the structural features (a) and (b) in

claim 1 were by themselves sufficient for achieving rapid dissolution. The same conclusion had been reached in decision T 1063/15, which concerned a related patent of the same patent family. Moreover, since the claimed dissolution profile described rapid dissolution, the claim was in any case limited to embodiments with rapid dissolution.

Thus, claim 1 as granted defined a product providing rapid release of the active agent cinacalcet. The claimed dissolution rate could only be achieved if the composition comprised components suitable for obtaining a dosage unit with the specified dissolution rate. This relationship was made even clearer in claim 1 of auxiliary request 6, which defined a composition in the form of a tablet (i.e. a dosage unit).

Starting from the disclosure in document D1, which did not describe any specific dosage form, the objective technical problem should be defined as the provision of an improved or rapid-release pharmaceutical composition of cinacalcet HCl.

The fact that cinacalcet was "sparingly soluble" and that its solubility was also pH-dependent (see the patent in suit, paragraph [0002]) meant that it presented difficulties for galenic formulation. Predictive modelling of dissolution behaviour was difficult (D75). The underlying problem formulated in the patent (paragraph [0003]) had been to maximise the release of cinacalcet HCl from dosage forms and to improve its bioavailability.

It was also known that phenylalkylamine-type calcimimetics (i.e. the class of actives to which cinacalcet belonged) were problematic due to unpredictable pharmacokinetics (see D1: page 1415, right-hand column, last paragraph). Thus, D1 itself raised concerns about this class. According to D1, only

one pharmacokinetic study of cinacalcet HCl had been published at the time of writing (page 1416, left-hand column, section 4.2).

Furthermore, the person skilled in the art would have had to consider that cinacalcet might be incompatible with some excipients.

Under these circumstances, the person skilled in the art, not having a reasonable expectation of success, would not have arrived at compositions as defined in claim 1 without employing inventive skill.

Secondary indicia also supported the presence of an inventive step, as the FDA and the scientific community had recognised that the commercial product Sensipar® covered by the patent in suit, an orphan drug for rare diseases, had fulfilled an unmet need in the medical community, and the product had received recognition as being a significant achievement in the industry.

XVI. The patent proprietor requested that the decision under appeal be set aside and that the patent be maintained as granted (i.e. that the oppositions be rejected),

or, alternatively, that the patent be maintained in amended form on the basis of the claims of auxiliary request 1 as filed with the patent proprietor's statement setting out the grounds of appeal,

or, in the alternative, that the opponents' appeals be dismissed and that the patent be maintained in amended form on the basis of the claims of auxiliary request 2 as submitted with the patent proprietor's reply (dated 8 August 2022) to the opponents' grounds of appeal,

or, in the further alternative, that the patent be maintained in amended form on the basis of the claims of one of auxiliary requests 3 to 10 as submitted with

the patent proprietor's reply to the opponents' grounds of appeal.

The patent proprietor also requested that documents D152 and D158 not be admitted. If D158 were to be admitted, then document D159 should also be admitted.

XVII. Opponent 2 requested that the decision under appeal be set aside and that the patent be revoked.

XVIII. Opponent 4 requested that the decision under appeal be set aside and that the patent be revoked. Opponent 4 also requested that documents D154 to D158 and document D124 be admitted. Furthermore, opponent 4 requested that auxiliary request 1 dated 21 March 2022 not be admitted.

XIX. Opponent 5 did not file any requests or substantive submissions during the appeal proceedings.

XX. Opponent 6 requested that the decision under appeal be set aside and that the patent be revoked.

XXI. Opponent 7 requested that the decision under appeal be set aside and that the patent be revoked. Opponent 7 also requested that document D158 be admitted.

XXII. Opponent 8 requested that the decision under appeal be set aside and that the patent be revoked. Furthermore, opponent 8 requested that auxiliary request 1 dated 21 March 2022 not be admitted.

XXIII. Opponent 10 requested that the decision under appeal be set aside and that the patent be revoked.

Reasons for the Decision

1. Oral proceedings, absent parties (Article 113(1) EPC)

1.1 In conformity with Rule 115(2) EPC and Article 15(3) RPBA, the oral proceedings before the board took place in the absence of opponents 5 and 6. Both had been duly summoned and had advised the board that they would not be attending (see section XII. above).

1.2 Opponent 5 had not presented any requests or arguments in writing. Thus, opponent 5 chose not to avail itself of the opportunity to present its comments on the grounds and evidence in the appeal case.

1.3 Opponent 6 was treated as relying only on his written case (Article 15(3) RPBA).

2. Claim construction

2.1 The composition according to claim 1 as granted (main request) is defined as comprising

(a) the pharmacologically active agent cinacalcet HCl within a certain concentration range (5-40 wt%) and

(b) an excipient comprising undefined amounts of microcrystalline cellulose and starch in a particular weight ratio (1:1-15:1).

In addition to these structural features, the claimed subject-matter is further defined by a dissolution profile of "at least one dosage unit". This functional feature requires "from 50% to 125% of a target amount of the cinacalcet being released from the composition no later than 30 minutes from the start of the test".

2.2 The parties had differing views on how the feature "at least one dosage unit" and the definition of the dissolution profile should be understood.

2.2.1 Opponent 8 pointed out that since claim 1 did not define the "target amount", this could be any portion of the cinacalcet present, including a minor portion. Thus, the definition of the dissolution profile in claim 1 covered a wide variety of embodiments and arguably did not require rapid release of the cinacalcet.

2.2.2 A further issue in dispute concerning the construction of claim 1 was the relationship between the claimed composition and the "at least one dosage unit".

While the claim defines a composition, the part of the claim that relates to the dissolution profile appears to be based on the premise that there is a plurality of dosage units.

In this context, it was questioned whether the wording "at least one dosage unit" required uniformity of the cinacalcet content and dissolution properties of multiple dosage units.

2.2.3 The opponents contended that since the dissolution profile did not have to apply to all dosage units, it did not have to apply across the claimed scope and should be ignored.

2.2.4 The patent proprietor was of the view that claim 1 as granted, as well as claim 1 of all of the auxiliary requests, defined a rapid dissolution profile, and that all dosage units were identical in terms of their dissolution properties, on account of being made from the claimed composition.

2.2.5 In the context of the debate relating to the inventive step of claim 1 as granted, the board arrived at the conclusion that the features defining the dissolution profile must apply to the "at least one dosage unit" as recited in the claim but not necessarily to any other dosage unit embodiment of claim 1, which implied that some embodiments did not have the functional limitation (see the minutes of the oral proceedings before the board, page 5, second paragraph).

2.3 At the oral proceedings before the board, inventive step within the meaning of Article 56 EPC was discussed in depth in relation to claim 1 as granted (main request) and again in relation to claim 1 of auxiliary request 6.

2.3.1 On account of the board's conclusion set out in section 2.2.5 above, the inventive step of claim 1 as granted was assessed without taking the dissolution profile into account. This resulted in the board finding that the subject-matter of claim 1 of the main request lacked an inventive step.

2.3.2 Claim 1 of auxiliary request 6 differs from claim 1 as granted in that it specifies that the composition is a tablet. The further difference that the dissolution test is to be conducted at 37°C rather than 37°C ± 0.5°C is irrelevant to the issue of inventive step.

The patent proprietor contended that on the basis of the definition in auxiliary request 6, it was in any case clear that the claimed pharmaceutical composition, the tablet and the "at least one dosage unit" were identical.

2.3.3 The discussion at the oral proceedings in relation to claim 1 of auxiliary request 6 was based on the patent proprietor's understanding of the claimed subject-matter, i.e. a pharmaceutical tablet having the structural features (a) and (b) and the dissolution profile as claimed (see the minutes of the oral proceedings before the board, page 7, sixth paragraph). This also included the further assumption that the claimed pharmaceutical composition had a rapid dissolution profile.

2.4 The board's inventive-step reasoning set out below is based on the assumptions made in relation to auxiliary request 6, which are in the patent proprietor's favour. Since this approach results in a finding of a lack of inventive step for the subject-matter of claim 1 of auxiliary request 6 (see section 3. below) and by extension also for the subject-matter of claim 1 of all other claim requests (see sections 4. to 7. below), a further detailed reasoning for alternative approaches to assessing inventive step is not required. Hence, for the purposes of this decision it is not necessary to set out the alternative considerations for claim 1 of the main request that do not take the dissolution profile into account (see section 2.3.1 above).

3. Inventive step - auxiliary request 6
(Articles 52(1) and 56 EPC)

3.1 In the interest of brevity, claim 1 of auxiliary request 6 is dealt with first. The relevance of the conclusions reached to the other claim requests is set out in sections 4. to 7. below.

Patent in suit

3.2 The patent in suit aims to provide pharmaceutical formulations of the active agent cinacalcet HCl. Since cinacalcet HCl is sparingly soluble in water, a need to maximise its dissolution is identified (see paragraphs [0001] and [0002] of the patent in suit).

3.3 The tablet defined in claim 1 of auxiliary request 6 contains a) 5-40% of cinacalcet HCl and b) an unspecified amount of microcrystalline cellulose (MCC) and starch in a ratio within the range of 1:1 to 15:1. The tablet has a dissolution profile which is presumed, for the purpose of the board's reasoning, to provide rapid dissolution in 0.05 N HCl under the conditions specified in claim 1 (see sections 2.3.3 and 2.4 above).

Starting point in the prior art

3.4 It was common ground that inventive step was to be assessed starting from the technical teaching of document D1, which reports results from various clinical studies, including phase III trials, about the use of cinacalcet HCl in the management of hyperparathyroidism.

3.5 These clinical studies used pharmaceutical compositions suitable for administration to human subjects. D1 states that cinacalcet HCl, also known as AMG 073, is an oral drug (see page 1413, first sentence of the abstract). Document D14, which is cited in D1 as reference [35], discloses that the medication in one of the studies mentioned in D1 was in the form of tablets (see D14: page 576, "Study Design", and the statement setting out the grounds of appeal of opponent 7, page 18).

3.6 Hyperparathyroidism is characterised by an elevated serum concentration of parathyroid hormone (PTH) (see D1: page 1413, second paragraph).

In one passage, D1 reports without reference to a particular study (see page 1416, left-hand column, 4.1), that

> "*PTH inhibition has occurred 2-4 h after the initial dose, with a duration of 18-24 h.*"

D1 further reports (see page 1417, left-hand column, first full paragraph) that in a single-dose and multi-dose study described in reference [32] of D1,

> "[*s*]*erum PTH at 2h of drug administration decreased by a maximum of 40, 54 and 55% in the 50, 75 and 100 mg doses of cinacalcet HCl, respectively*".

Furthermore, D1 reports (see page 1419, left-hand column, first full paragraph) that in certain studies, hypocalcaemia as a side effect

> *"[...] usually occurred between 30 min and 12 h after drug administration [...]".*

While several passages in D1 thus suggest that the active agent was available in the body soon after administration, it is not known how the respective study drugs would have performed in a USP test as defined in claim 1 (United States Pharmacopeia, see paragraphs [0006] and [0007] of the patent in suit).

Distinguishing technical features and technical effects

3.7 Since D1 does not disclose a specific product formulation for the study medications, the following technical features distinguish the subject-matter of claim 1 from the disclosure in D1:

(a) the concentration range of 5-40% by weight specified for cinacalcet HCl

(b) the presence of microcrystalline cellulose, the presence of starch, and the range of 1:1 to 15:1 specified for the weight ratio of microcrystalline cellulose to starch

(c) the specified dissolution profile

Arguably, the tablet form may not be a distinguishing feature since it is disclosed in D1 by reference to the study of D14. Table 3 in D1 includes the study presented in reference [35], also mentioned on page 1417 of D1 (right-hand column, end of first paragraph). Reference [35] of D1 is, as stated above, D14 in these appeal proceedings. D14 discloses the following on page 576, in the section on "Study Design":

> *"AMG 073 and placebo tablets were manufactured for Amgen and were identical in appearance to maintain the double-blind status of the study."*

Thus, at least one study discussed in D1 used tablets as the dosage form of its study medication.

In any case, the tablet form was a known option that provides a specific oral dosage form for putting a pharmaceutical formulation of cinacalcet HCl into practice. So even if the tablet form is considered to be a distinguishing feature, as also addressed in the reasoning below (see section 3.14), it cannot provide the basis for an inventive step.

3.8 No specific technical effect can be attributed to the structural features (a) and (b).

Feature (a) merely reflects the requirement that the pharmacologically active agent cinacalcet HCl be present in the tablet in a suitable amount.

As far as feature (b) is concerned, while starch and microcrystalline cellulose are known as tablet disintegrants (see D4a: pages 174 and 175), claim 1 does not define minimum concentrations for these components. As a consequence, tablet disintegration, or any other property of the tablets for that matter, is not necessarily determined by these components (or the ratio thereof) in all the embodiments covered by claim 1.

Contrary to the patent proprietor's view, it is not appropriate to read lower concentration limits into the claim on the basis of the excipient concentrations disclosed in the description of the example formulation (see paragraph [0057]).

The further passage in paragraph [0035] of the patent, also relied on by the patent proprietor, reads as follows:

> *"The microcrystalline cellulose can be present in an amount ranging from about 25% to about 85% (...) The starch can be present in an amount ranging from about 5% to about 35% (...)."*

These concentration ranges are disclosed as optional, as indicated by the use of the formulation *"can be present"*, and in any case this passage cannot overrule the absence of lower concentration limits in the claim itself.

Thus, claim 1 also encompasses embodiments with only minor, i.e. negligible, amounts of starch and microcrystalline cellulose. In such embodiments, the weight ratio would also have no technical effect.

There is no evidence of any specific technical effect that could be attributed to feature (b) across the whole claimed scope.

As structural features (a) and (b) taken together may leave almost 95% by weight of the claimed composition undefined, the assumption that these features alone would guarantee any particular dissolution profile is not justified. Hence, the board does not see a causal relationship between structural features (a) and (b) and the dissolution profile defined in claim 1. Rather, the dissolution profile is an additional - functionally defined - requirement.

3.9 The situation in decision T 1063/15 (relied on by the patent proprietor in support of the view that features (a) and (b) in claim 1 should be accepted as sufficient for achieving rapid dissolution) was different in that the claim considered in that decision specified that microcrystalline cellulose must be present at 40% to 75% by weight and starch at 5% to 10% by weight. The claim did not include a dissolution profile. According to an experimental report, compositions as claimed had been shown to achieve rapid dissolution. In the absence of counter-evidence, the competent board accepted that the claimed compositions achieved rapid dissolution.

In the present case, due to the absence of lower concentration limits in the claim, evidence would have been required to show that the excipients in feature (b) can achieve any alleged technical effect even at low concentrations, as this does not seem technically credible.

3.10 Irrespective of these considerations, claim 1 of the current auxiliary request 6 also defines a dissolution profile, which is a further distinguishing feature in comparison with the disclosure of D1 (see feature (c) in section 3.7 above). As already mentioned, the board's considerations are based on the assumption, in

the patent proprietor's favour, that the dissolution profile in claim 1 is understood as conferring rapid dissolution, and hence, that rapid dissolution is a technical effect attained by the claimed tablet across the whole scope claimed.

Objective technical problem and solution

3.11 Based on this assumption, the objective technical problem to be solved is the provision of a specific oral pharmaceutical composition of cinacalcet HCl with rapid dissolution.

3.12 The objective technical problem cannot be defined as the provision of an "improved" composition, as there is no evidence that the compositions as claimed have any improved property in comparison with compositions as administered in the clinical trials disclosed in D1 (see section 3.5 above).

3.13 The claimed solution to the objective technical problem cannot be seen as a mere statement of a dissolution profile as a desideratum. Rather, the solution is provided by the dissolution profile together with the overall galenic formulation of the claimed tablet, which, in addition to providing a specific oral pharmaceutical composition of cinacalcet HCl, has to be chosen in such a way that the claimed tablet achieves rapid dissolution in accordance with the dissolution profile. This overall formulation includes the components mentioned in items (a) and (b) of claim 1 and up to almost 95% by weight of further components not identified in the claim.

Obviousness of the solution

3.14 D1 mentions that cinacalcet HCl is an oral drug. Even if the tablet form were considered to be a distinguishing feature over D1, tablets were the dosage form of choice for oral pharmaceutical compositions, because of ease of manufacture and administration. Moreover, tablets were known to have been used in the study of D14, referenced in D1.

3.15 The chosen concentration of 5% to 40% by weight of cinacalcet HCl was a typical concentration for the pharmacologically active agent in a pharmaceutical tablet formulation, known to provide a quantity suitable for both manufacture and dosing.

3.16 The use of typical pharmaceutical tablet excipients such as starch and microcrystalline cellulose, being common in galenic formulation (see D10, pages 483 to 488; D10a, pages 84 to 87), would also have been considered for the purpose of providing a specific composition of cinacalcet HCl. Since both components were known *inter alia* as tablet disintegrants (see D10, page 483, right-hand column, section 6; D10a, page 84, left-hand column, section 6; D4a, pages 174 and 175) their use would not have been expected to be contrary to the aim of achieving rapid dissolution. There was also no reason to avoid working with a weight ratio between 1:1 and 15:1.

3.17 Thus, neither the concentration range in feature (a) nor feature (b) of claim 1 represents an unusual, non-obvious choice.

3.18 As far as the aim of rapid dissolution is concerned, the following considerations are of relevance:

3.19 Selecting a dissolution profile that provides rapid release would have been an obvious measure for the person skilled in the art seeking to solve the objective technical problem.

3.20 Claim 1 does not define a complete formulation by indicating all components with their concentrations adding up to 100%. In other words, claim 1 does not actually identify the technical features necessary for achieving the dissolution profile recited in the claim.

3.21 However, optimising tablet formulations so as to achieve a desired dissolution profile was a routine activity in the field of galenic formulation, typically following a standard process. Using common general knowledge, the person skilled in the art would have been capable of providing formulations of cinacalcet HCl exhibiting rapid dissolution, e.g. according to the dissolution profile defined in claim 1.

3.22 There is no reason to assume that this would have been possible only by non-obvious, unusual measures (choices of excipients, particle sizes, manufacturing techniques, etc.). If this had indeed been the case, it would have been essential that these features were included in claim 1. If the means by which the desired release type was to be achieved were not obvious to the skilled person, this could also raise questions about whether or not the claimed invention was sufficiently disclosed under Article 83 EPC.

3.23 The patent proprietor argued that the person skilled in the art would nevertheless not have had a reasonable expectation of success, for the following reasons.

(a) As set out in paragraph [0002] of the patent in suit, cinacalcet HCl was only sparingly soluble in water. This would have made it particularly difficult to provide formulations with rapid dissolution and good bioavailability, especially as predictive modelling of *in vitro* dissolution was still considered difficult even years after the priority date of the patent (see D75).

(b) The person skilled in the art would also have been deterred by potential incompatibilities between cinacalcet HCl and excipients.

(c) D1 itself mentioned that phenylalkylamine-type calcimimetics (i.e. the class of actives to which cinacalcet belonged) were problematic due to unpredictable pharmacokinetics (see D1: page 1415, right-hand column, last paragraph). According to D1, only one pharmacokinetic study of cinacalcet HCl had been published at the time of writing (page 1416, left-hand column, section 4.2).

3.24 These arguments cannot succeed for the following reasons.

(a) Providing functional solid oral formulations of sparingly soluble active agents was a routine task for the pharmaceutical chemist. No reason was provided as to why the skilled person would have considered this task to be unusually difficult in the case of cinacalcet HCl, to the extent that they would have had no reasonable expectation of success. Predictive dissolution modelling, an "emerging methodology" presented in D75 (see page 32, line 13), would not have been needed to accomplish this task, since the usual methodology, i.e. actual dissolution testing, was available.

(b) No specific incompatibility of cinacalcet HCl was identified. The fact that microcrystalline cellulose and starch may be incompatible with strongly oxidising substances would not have been a concern in the case of cinacalcet HCl, which is not a strongly oxidising substance. There was no specific reason for the skilled person to expect a high incidence of excipient incompatibility in the case of cinacalcet HCl. In any case, general caution required that the stability of a drug be determined with each proposed excipient (see D4a, page 133, last paragraph). This was a general requirement in pharmaceutical development, which was not only applicable to cinacalcet HCl, and which would not have been considered to be an insurmountable obstacle in any case.

(c) The negative comments on page 1415 of D1 relate to first-generation phenylalkylamine calcimimetics, whereas cinacalcet HCl is a second-generation calcimimetic. D1 discloses that cinacalcet HCl has a favourable pharmacokinetic profile compared to its precursors and had entered the stage of clinical phase-III testing (see D1: abstract; page 1415, last paragraph; page 1416, first paragraph). The person skilled in the art studying D1 would thus have been fairly optimistic about the therapeutic use of cinacalcet HCl. The patent proprietor's argument also fails for the more fundamental reason that the objective technical problem already specifies the active agent.

3.25 For these reasons, the claimed composition would have been obvious to the skilled person seeking to solve the objective technical problem.

3.26 The patent proprietor also submitted that there were secondary indicia in favour of an inventive step. The commercial product covered by the patent in suit had received designations as an orphan drug for the treatment of secondary hyperparathyroidism in dialysis patients and for other indications, i.e. as fulfilling an unmet need, and had received recognition as being a significant achievement in the industry.

3.27 This argument fails for the following reasons:

Secondary indicia may sometimes be considered in cases of doubt, i.e. when objective evaluation of the prior-art teachings does not present a clear picture. Their presence does not necessarily confer inventiveness on the claimed subject-matter.

Considerations based on the presence of secondary indicia cannot replace the objective assessment of inventive step following the problem-and-solution approach. In the case at hand, the assessment according to the problem-and-solution approach shows conclusively that the claimed subject-matter does not involve an inventive step.

Furthermore, the prior knowledge about the expected efficacy of cinacalcet HCl is summarised in D1. The claimed invention is not about selecting cinacalcet HCl for therapeutic use to meet a long-felt need, but about providing a suitable composition for administering it. The advantages mentioned by the patent proprietor as secondary indicia are not pertinent since they are not necessarily linked to any difficulties that had to be overcome in providing the claimed composition.

D1 was published in 2003, i.e. shortly before the priority date of the patent in suit. According to D1, cinacalcet HCl was at that time still an investigational drug. D1 also discloses that

compositions of cinacalcet HCl had been prepared for various studies, including in the form of tablets (see D14). Thus, at the relevant date there was already an interest in developing cinacalcet HCl. There was not a long time gap before the claimed composition was put into practice. There is thus no convincing evidence that providing a functional pharmaceutical composition of cinacalcet HCl would have presented particular difficulty to the person skilled in the art.

3.28 For these reasons, the subject-matter of claim 1 of auxiliary request 6 does not involve an inventive step within the meaning of Article 56 EPC.

4. Inventive step - main request (Articles 100(a), 52(1) and 56 EPC)

4.1 The reasoning and negative conclusion on inventive step set out above in relation to claim 1 of auxiliary request 6 (see section 3.) also applies to claim 1 of the main request, since claim 1 of auxiliary request 6 is more limited in scope than claim 1 as granted. The assessment provided for claim 1 of auxiliary request 6 also applies to the case where the at least one dosage form in claim 1 of the main request is a tablet.

4.2 As a consequence, the subject-matter of claim 1 of the main request does not involve an inventive step within the meaning of Article 56 EPC. The ground for opposition under Article 100(a) and Articles 52(1) and 56 EPC therefore prejudices the maintenance of the patent as granted.

5. Inventive step - auxiliary requests 1 and 2

5.1 As already mentioned, claim 1 of auxiliary requests 1 and 2 is identical to claim 1 of the main request (see sections IX. and X. above). Hence, the same

considerations and conclusion on inventive step apply to these claims as set out in section 4. with respect to claim 1 of the main request.

5.2 As a consequence, the subject-matter of claim 1 of auxiliary requests 1 and 2 does not involve an inventive step within the meaning of Article 56 EPC.

5.3 In view of this outcome on the merits of auxiliary request 1, it is not necessary to provide reasoning for the admittance of auxiliary request 1.

6. Inventive step - auxiliary requests 3 to 5, 7 and 8

6.1 Claim 1 of auxiliary requests 3 to 5 (see section X. above) only differs from claim 1 of the main request by defining the temperature at which the dissolution test is to be conducted as "37°C" rather than "37°±0.5°C" (auxiliary requests 3 and 5) and/or by specifying that the composition is in a form chosen from tablets and capsules (auxiliary requests 4 and 5).

6.2 Claim 1 of auxiliary requests 7 and 8 is the same as claim 1 of auxiliary request 5, except that in auxiliary request 7 the percentage of the target amount to be released within 30 minutes is 85% to 125% and in auxiliary request 8 it is 85% to 100% (see section X. above).

6.3 None of these modified or added technical features requires any modification to the reasoning provided in sections 3 and 4 above in relation to inventive step. The options that the composition may be a tablet or capsule include the option that it is a tablet, which was found not to be inventive. Since the board based its considerations on the general assumption that the dissolution profile amounts to rapid dissolution, the permitted temperature variation in the dissolution test

or the exact proportion of substance released within 30 minutes makes no difference to the inventive-step reasoning set out above.

6.4 As a consequence, the subject-matter of claim 1 of each of auxiliary requests 3, 4, 5, 7 and 8 does not involve an inventive step within the meaning of Article 56 EPC.

7. Inventive step - auxiliary requests 9 and 10

7.1 Claim 1 of auxiliary requests 9 and 10 is the same as claim 1 of auxiliary request 6, except that in auxiliary request 9 the percentage of the target amount to be released within 30 minutes is 85% to 125% and in auxiliary request 10 it is 85% to 100% (see section X. above).

7.2 Neither of these modified technical features requires any change to the reasoning provided in section 3. above in relation to inventive step.

7.3 As a consequence, the subject-matter of claim 1 of auxiliary requests 9 and 10 does not involve an inventive step within the meaning of Article 56 EPC.

8. Requests concerning the admittance of evidence

Documents D124 and D152 to D158 were all filed by the opponents (see sections V. and XI. above). Document D124 had also previously been filed in the proceedings before the opposition division. The board's reasoning set out above, which resulted in the revocation of the patent in suit, does not rely on any of these documents. Thus, it was not necessary for the board to decide on their admittance. Moreover, it was not necessary to decide on the admittance of document D159,

either, because it was filed by the patent proprietor specifically in response to D158.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

C. Rodríguez Rodríguez M. Pregetter

Decision electronically authenticated