Internal distribution code:

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

Datasheet for the decision of 11 June 2026

Case Number: T 1087/24 - 3.3.07

Application Number: 18206195.2

Publication Number: 3461484

IPC: A61K31/47, A61K31/557, A61P27/06

Language of the proceedings: EN

Title of invention:

DIMESYLATE SALTS OF 4-(3-AMINO-1-(ISOQUINOLIN-6-YLAMINO)-1-OXOPROPAN-2-YL)BENZYL, THEIR COMBINATIONS WITH PROSTAGLANDINS AND THE USE THEREOF IN THE TREATMENT OF OCULAR DISORDERS

Patent Proprietor:

ALCON INC.

Opponents:

Alfred E. Tiefenbacher (GmbH & Co. KG)
Isarpatent - Patent- und Rechtsanwälte Barth
Charles Hassa Peckmann und Partner mbB
df-mp Dörries Frank-Molnia & Pohlman
Patentanwälte Rechtsanwälte ParG mbB

Headword:

Dimesylate salts/ALCON

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

Keyword:
Inventive step - obvious alternative - improvement not credible
Amendment after notification of Article 15(1) RPBA communication - exceptional circumstances (no)

Decisions cited:
T 0536/07, T 0184/16

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

Case Number: T 1087/24 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 11 June 2026

Appellant: (Opponent 2)	Isarpatent - Patent- und Rechtsanwälte Barth Charles Hassa Peckmann und Partner mbB Friedrichstrasse 31 80801 München (DE)
Representative:	Isarpatent Patent- und Rechtsanwälte Barth Charles Hassa Peckmann & Partner mbB Friedrichstrasse 31 80801 München (DE)
Appellant: (Opponent 3)	df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte ParG mbB Fünf Höfe Theatinerstrasse 16 80333 München (DE)
Representative:	Greiner, Elisabeth df-mp Patentanwälte Rechtsanwälte PartG mbB Theatinerstraße 16 80333 München (DE)
Respondent: (Patent Proprietor)	ALCON INC. Rue Louis-d'Affry 6 1701 Fribourg (CH)
Representative:	K&L Gates LLP Friedrichstraße 110 A 10117 Berlin (DE)
Party as of right: (Opponent 1)	Alfred E. Tiefenbacher (GmbH & Co. KG) Van-der-Smissen-Str. 1 22767 Hamburg (DE)

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

Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted/ electronically transmitted on 1 July 2024 concerning maintenance of the European Patent No. 3461484 in amended form.**

Composition of the Board:

Chairman A. Usuelli
Members: M. Steendijk
Y. Podbielski

Summary of Facts and Submissions

I. European patent 3 461 484 ("the patent") was granted with thirteen claims.

The claims as granted relate to the compound 4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl) benzyl 2,4-dimethylbenzoate dimesylate, as the racemate or as the individual R- or S-enantiomer, including claims directed to a composition comprising this compound and a prostaglandin selected from a defined group of agents, and the composition or compound for use in treating an ocular disorder, in particular glaucoma, or for use in reducing intraocular pressure (IOP).

The S-enantiomer of the defined compound was assigned the INN netarsudil.

II. Three oppositions were filed against the grant of the patent on the grounds that its subject-matter lacked novelty and inventive step, that the claimed invention was not sufficiently disclosed and that the patent comprised subject-matter extending beyond the content of the original parent application and the application as filed.

The opposition division decided that the patent as amended in accordance with auxiliary request 1, filed during the oral proceedings held on 23 May 2024, meets the requirements of the EPC.

Claim 1 of this request defines:

"A composition comprising:
a) (rac)-4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate dimesylate; and
b) a prostaglandin selected from the group consisting of: latanoprost; bimatoprost; travoprost; tafluprost; AR-102; cloprostenol isopropyl ester; 13,14-dihydrocloprostenol isopropyl ester; latanoprostene bunod; unoprostone; PGF1α isopropyl ester; PGF2α isopropyl ester; PGF3α isopropyl ester; fluprostenol isopropyl ester; or a pharmaceutically acceptable salt thereof."

Independent claims 3 and 5 correspond to claim 1, except that the compound defined under a) in claim 1 is the R- and S-enantiomer, respectively.

Independent claims 8-10 define a compound as such, wherein the compound is, respectively, the R-isomer, the S-isomer or the racemate of the compound defined under a) in claim 1.

Claims 11 and 12 define the composition of any one of claims 1-7 for use in treating an ocular disorder in a subject in need thereof wherein the ocular disorder is glaucoma (claim 11), or for use in reducing intraocular pressure in a subject in need thereof (claim 12).

The following documents were *inter alia* cited:

D2: EP 1 541 151 A1
D6: US 8,394,826 B2

D7: Journal of Medicinal Chemistry (2007), 50, 6665-6672
D12: Pharmaceutical Technology (2008), 32(3),"Salt selection in Drug Development"
D14: Journal of Pharmaceutical Sciences (1977), 66(1), 1-19
D21: Recent patents on Endocrine Metabolic & Immune Drug Discovery (2012), 6, 89-98
D30: Remington's Pharmaceutical Sciences, 1985 (17th ed.), 1418-1419
D31: Journal of Pharmaceutical Sciences (2010), 99(7), 2948-2961
D32: EP 2 671 586 A1.

The opposition division arrived at the following conclusions:

(a) The patent as granted did not sufficiently disclose the utility of the defined composition for the treatment of an ocular disease in general as defined in claim 11 as granted.

(b) Auxiliary request 1 complied with Articles 76(1), 123(2), 83 and 54 EPC.

Document D6 represented the closest prior art. The document described structurally defined Rho-kinase inhibitors, including 4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate and its dihydrochloride.

The difference between the claimed subject-matter and the closest prior art concerned the type of netarsudil salt.

The supplemental experimental data submitted on 3 October 2019 during the examination proceedings showed that netarsudil dimesylate achieves a greater reduction of intraocular pressure than the dihydrochloride (Figure 2) and the di-L-aspartate (Figures 3 and 4). In view of this evidence, the objective technical problem was the provision of an improved composition for reducing intraocular pressure and treating glaucoma. The claimed solution was not obvious to the skilled person in the light of the prior art.

Auxiliary request 1 therefore also complied with Article 56 EPC.

III. Opponent 2 (O2) and opponent 3 (O3) filed appeals against the interlocutory decision of the opposition division that the patent, as amended in accordance with auxiliary request 1, meets the requirements of the EPC.

IV. With the reply to the appeals, the patent proprietor maintained the request held allowable by the opposition division as its main request and filed a number of auxiliary requests.

V. In its communication pursuant to Article 15(1) RPBA, the Board summarized the objections raised in the statements of grounds of appeal by O2 and O3, that the supplemental experimental data in the submission of 3 October 2019 did not provide convincing evidence that the choice of the dimesylate salt of netarsudil constituted an improvement over the dihydrochloride salt described in document D6, in view of the lack of essential information and the absence of any demonstrated consistent improvement.

The Board further observed that, in its reply, the patent proprietor submitted that the supplemental experimental data filed on 3 October 2019 clearly demonstrated that the use of netarsudil dimesylate allowed an improved reduction of intraocular pressure compared with the dihydrochloride, but did not appear to address the specific objections raised by the opponents as to the relevance and consistency of the presented results.

In view of these objections, the Board was not convinced of the relevance and significance of those results and expressed the preliminary opinion that the objective technical problem cannot be formulated as an improvement over the dihydrochloride and is instead to be formulated in terms of an alternative.

VI. With its submission of 16 March 2026 the patent proprietor maintained that the supplemental experimental data filed on 3 October 2019 clearly demonstrated the improvement associated with the choice of the dimesylate salt of (S)-netarsudil over the dihydrochloride. With the same submission, the patent proprietor also filed the following additional document:

A41: Statement of Meredith Weksler of 31 October 2025, including "IOP study of 0.05% AR-13324 as diHCl or dimesylate salt form".

VII. Oral proceedings were held on 11 June 2026. Following the Board's decision not to admit document A41, the patent proprietor requested that the case be remitted to the opposition division. During the oral proceedings, the patent proprietor withdrew its auxiliary requests filed with the reply to the appeals.

VIII. The arguments of the opponents relevant to the present decision are summarized as follows:

- Admittance of document A41

  O3 raised, during the proceedings before the opposition division on 13 December 2022, the objection that the supplemental experimental data filed on 3 October 2019 did not demonstrate an advantage of the dimesylate salt over the known dihydrochloride salt of netarsudil, in view of the lack of information regarding the experimental setting and the absence of a demonstrated consistent improvement. This objection was maintained in O3's statement of grounds of appeal. No exceptional circumstances justified the admission of document A41, which was filed after the Board's communication under Article 15(1) RPBA to address that objection. Moreover, document A41 lacked *prima facie* relevance, as it did not appear to demonstrate a consistent improvement for the dimesylate salt.

- Inventive step

  The burden of proof lay with the patent proprietor to demonstrate that the choice of the dimesylate salt of netarsudil over the dihydrochloride salt known from document D6 was associated with an unexpected improvement. The supplemental experimental data filed on 3 October 2019 did not convincingly demonstrate such an advantage. The relevance of the results could not be verified, as essential information was not provided. Moreover,

the results did not show any consistent improvement of the dimesylate salt over the dihydrochloride. The objective technical problem therefore concerned the provision of an alternative salt of netarsudil. The choice of the dimesylate salt as a solution to that problem was obvious to the skilled person, in view of the common use of mesylate salts for pharmaceutically active agents, as evidenced by documents D12, D14, D30 and D31.

IX. The arguments of the patent proprietor relevant to the present decision are summarised as follows:

- Admittance of document A41

The declaration and experimental report in document A41 confirmed the improvement associated with the dimesylate salt of netarsudil over the dihydrochloride and addressed the opponents' objection concerning the absence of detailed information on the experimental conditions underlying the supplemental data filed on 3 October 2019. Following the transfer of the patent from Aerie Pharmaceuticals to Alcon in 2022, the patent proprietor was not in a position to provide the precise experimental details of the 2019 tests. The opponents' objection had been pursued only at a late stage of the proceedings before the opposition division and had not affected its outcome. The opponents had not provided any counter-evidence capable of raising serious doubts as to the validity of the data filed on 3 October 2019. According to established case law (Case Law of the Boards of Appeal, 11th ed. 2025, I.D.4.3.2; T 536/07; T 184/16), such evidence was required to substantiate the objection. The patent

proprietor could therefore not reasonably be expected to file the evidence in document A41 with its reply to the appeals. The filing of document A41 thus constituted a legitimate response to the Board's preliminary opinion, and exceptional circumstances justified its admission.

- Request for remittal to the opposition division

The remittal of the case was justified in order to allow the opposition division to assess document A41 in detail.

- Inventive step

The supplemental experimental data filed on 3 October 2019 showed in Figures 2 to 4 a consistent improvement in the reduction of intraocular pressure resulting from the choice of the dimesylate salt of netarsudil over the dihydrochloride salt known from document D6. The skilled person was able to verify this improvement on the basis of common general knowledge relating to intraocular pressure-lowering formulations and corresponding animal models. Moreover, Example 9 of the patent provided guidance for the preparation of such formulations. In view of these data, and in accordance with established case law, the burden of proof rested on the opponents to provide evidence capable of raising serious doubts as to the demonstrated improvement. The opponents did not discharge that burden, as they did not submit any experimental results of their own or any expert declaration. The objective technical problem therefore concerned the provision of an improved salt of netarsudil. As shown in document D7,

hydrochloride salts were by far the most commonly used acid addition salts for basic active pharmaceutical ingredients, whereas mesylate salts were relatively uncommon. The prior art thus provided no motivation to select the dimesylate salt of netarsudil as an alternative, let alone as an improvement over the known dihydrochloride.

X. The appellants-opponents requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

O3 further requested that document A41 not be admitted into the appeal proceedings.

XI. The respondent-patent proprietor requested that the appeals be dismissed and the patent be maintained on the basis of the request held allowable by the opposition division (main request).

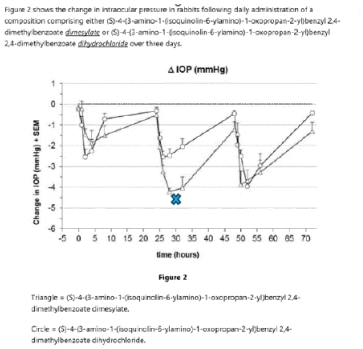
The patent proprietor further requested that document A41 be admitted into the appeal proceedings. The patent proprietor also requested that the case be remitted to the opposition division for further prosecution.

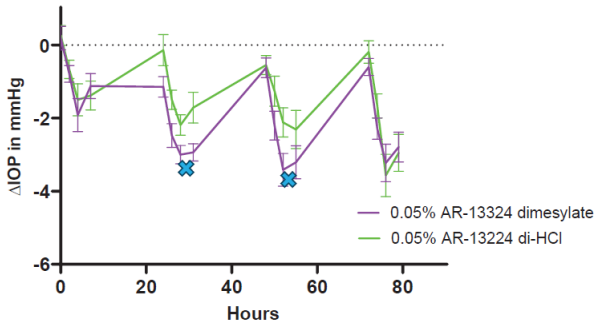
Reasons for the Decision

1. Admittance of document A41

1.1 Document A41 comprises an expert declaration by Meredith Weksler and an experimental report relied on by the patent proprietor to confirm the improved reduction of intraocular pressure (IOP) associated with the dimesylate salt of netarsudil over the dihydrochloride known from the prior art. In the declaration, the expert states that new experiments

were carried out in 2025 using the same experimental protocol as that employed to generate the supplemental experimental data filed in 2019 contested by the opponents. The experimental report sets out the details of the experimental set-up for these new experiments and, as indicated below, it presents the results (right graphic) alongside Figure 2 in the supplemental data of 2019 (left graphic):





Document A41 was filed after notification of the Board's communication under Article 15(1) RPBA and is therefore, in principle, not to be taken into account pursuant to Article 13(2) RPBA, unless there are exceptional circumstances justified with cogent reasons.

1.2 The patent proprietor justified the filing of document A41 as a legitimate response to the Board's preliminary opinion in the communication pursuant to Article 15(1) RPBA concerning the relevance and significance of the supplemental experimental data filed in 2019.

However, the Board's communication (section 5.2.2) merely summarised the objections in the opponents' statements of grounds of appeal, namely that, in the absence of information on the experimental setting and of a demonstrated consistent improvement, the data

filed on 3 October 2019 did not constitute convincing evidence of an improvement of the claimed dimesylate salt over the known dihydrochloride. It further indicated (section 5.2.3) that these objections did not appear to have been specifically addressed in the patent proprietor's reply, so that the Board was not convinced of the relevance and significance of the supplemental experimental data from 2019. Notably, these objections had first been raised during the proceedings before the opposition division by O3, in advance of the oral proceedings, with its submission of 13 December 2022 (see in particular paragraphs 35-40).

Accordingly, neither the opponents' statement of grounds of appeal nor the Board's communication introduced any new issue or otherwise gave rise to exceptional circumstances within the meaning of Article 13(2) RPBA that could justify the admittance of document A41.

1.3 The circumstance that, following the transfer of the patent in 2022, the patent proprietor was not in a position to provide the precise experimental details of the 2019 tests falls within its sphere of responsibility and cannot justify the late filing of document A41.

The argument that the opponents had not provided counter-evidence capable of raising serious doubts as to the validity of the data filed on 3 October 2019 merely concerns the assessment of the relevance and probative value of those data and likewise does not justify the late filing of document A41.

1.4 Even if the Board were to adopt a very broad interpretation of the "exceptional circumstances", then

this would not lead to the admittance of A41 either. The new experimental results reported in document A41 appear to indicate a greater reduction of IOP for the dimesylate salt compared to the dihydrochloride following administration on days 2 and 3, but only a similar or smaller reduction on days 1 and 4. By contrast, Figure 2 of the 2019 data appears to indicate a similar or smaller reduction following administration of the dimesylate salt on day 3. It therefore appears questionable whether the experimental data in document A41 actually demonstrate a consistent improvement for the dimesylate. Accordingly, document A41 is not *prima facie* suitable to support a consistent improvement for the dimesylate salt.

1.5 The Board therefore did not admit document A41 into the appeal proceedings under Article 13(2) RPBA.

2. Request for remittal

2.1 Following the Board's decision not to admit document A41 into the appeal proceedings, the patent proprietor requested remittal of the case to the opposition division to allow the assessment of document A41 in detail.

2.2 Remittal of the case in order to allow the opposition division to assess document A41 in detail is not justified. Since document A41 was not admitted into the appeal proceedings under Article 13(2) RPBA, it does not form part of the proceedings and thus provides no basis for further examination. Remittal for the sole purpose of enabling the opposition division to examine a document that has not been admitted into the proceedings would be contrary to the procedural framework laid down in Article 13(2) RPBA and would

undermine the principle of procedural economy. Accordingly, no special reasons within the meaning of Article 11 RPBA justify remittal.

2.3 The Board therefore refused the request for remittal.

3. Inventive step

3.1 Starting point in the prior art

It was not in dispute that document D6 represents a suitable starting point in the prior art for the assessment of inventive step.

Document D6 describes the racemate of the netarsudil compound and its dihydrochloride salt, as well as individual isomers thereof, as examples of substituted isoquinoline amide compounds with utility in the treatment of glaucoma (see D6, column 1, lines 13-22; column 47 compounds E145/E146; columns 53-54 example 197). Document D6 explains that inhibitors of Rho kinase reduce intraocular pressure and suggests that the beneficial activity of the described compounds may, in part, be attributed to the Rho kinase modulating activity of the described compounds (see D6, column 2 lines 5-52). Document D6 further mentions that the described compounds may be administered in conjunction with a variety of additional therapeutic agents, including prostaglandin-like compounds such as latanoprost (see D6, column 17 lines 55-60 and column 18, line 6).

It was also undisputed that the difference between the subject-matter of claims 8-10 and the teaching in document D6 concerns the nature of the defined netarsudil salt, namely the dimesylate instead of the

dihydrochloride, and that the subject-matter of claims 1-7 and 11-12 is additionally distinguished by the combination with a prostaglandin compound selected from the defined group.

3.2 Objective technical problem

3.2.1 In order to determine the objective technical problem, it must first be established whether the distinguishing feature, namely the replacement of the dihydrochloride by the dimesylate salt, provides a technical effect over the closest prior art.

3.2.2 The patent (see, for example, paragraph [0020]) teaches that the disclosed compounds, including the racemate and the individual isomers of netarsudil, alone or in compositions comprising a prostaglandin or prostaglandin analog, may be effective for the treatment of glaucoma and for reducing IOP. The patent further discloses a single example specifically directed to the dimesylate salt of netarsudil (Example 9, paragraphs [0146]-[0147]), in which the effective treatment of a human subject diagnosed with elevated IOP is reported using a formulation comprising the dimesylate salt of netarsudil (0.02%) and latanoprost (0.005%), together with excipients.

However, the patent itself does not provide any comparative data for the dimesylate salt and the dihydrochloride.

3.2.3 The patent proprietor relied on the below reproduced sections of the supplemental experimental data relating to Figures 2-4, filed on 3 October 2019, as evidence of an improvement associated with the dimesylate salt of netarsudil over the dihydrochloride.

Figure 2 shows the change in intraocular pressure in rabbits following daily administration of a composition comprising either (S)-4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate *dimesylate* or (S)-4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate *dihydrochloride* over three days.

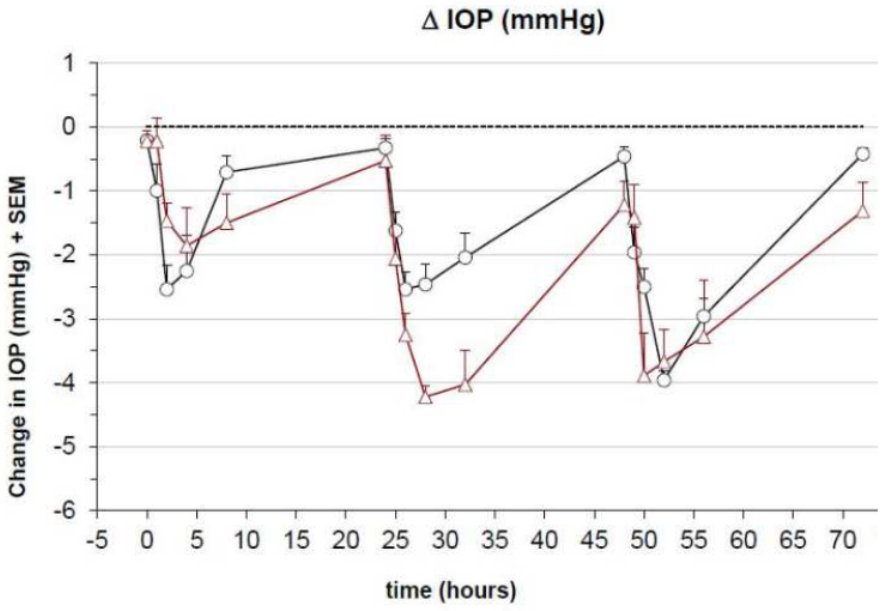


Figure 2

Triangle = (S)-4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate dimesylate.

Circle = (S)-4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate dihydrochloride.

As can be seen from Figure 2, the claimed dimesylate salt form unexpectedly improved the reduction in intraocular pressure when administered to rabbits as compared to the dihydrochoride salt form.

Figures 3 and 4 show the change in intraocular pressure in rabbits following daily administration of a composition comprising either (S)-4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate ***dimesylate*** (Figure 3) or (S)-4-(3-amino-1-(isoquinolin-6-ylamino)-1-oxopropan-2-yl)benzyl 2,4-dimethylbenzoate ***di-L-aspartate*** (Figure 4) over three days.

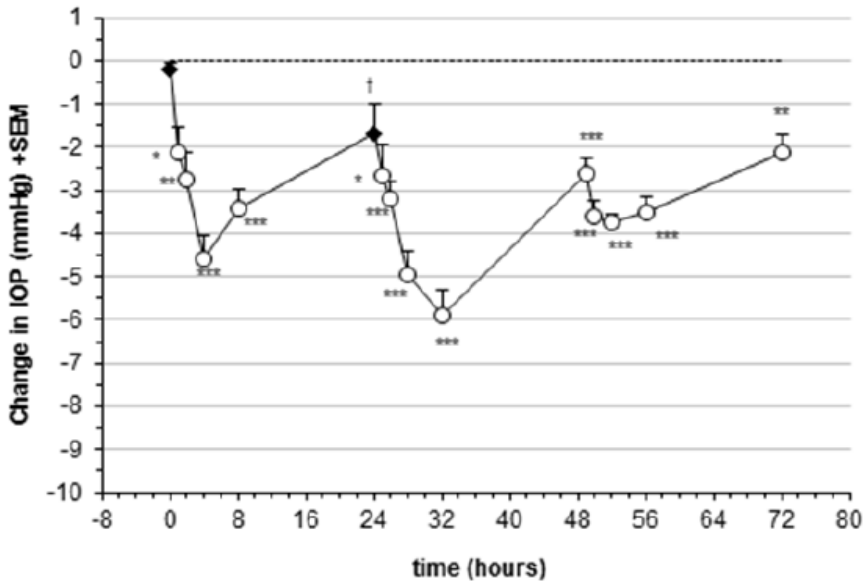


Figure 3

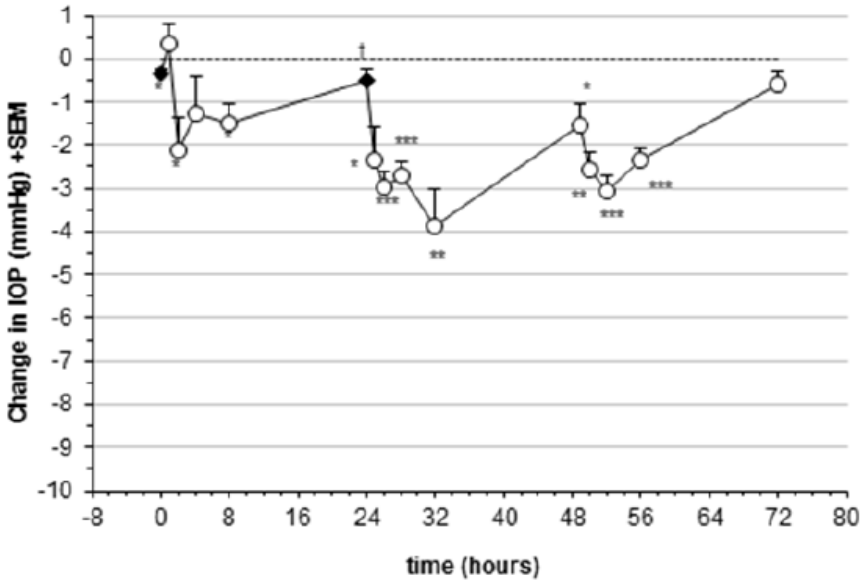


Figure 4

As can be seen from Figures 3 and 4, the claimed dimesylate salt form improved the reduction in intraocular pressure when administered to rabbits as compared to the corresponding di-L-aspartate salt form.

The patent proprietor submitted that these data clearly demonstrated a consistent improvement in the reduction of IOP over three days of administration and that, in

view of these data, the burden of proof to the contrary rested on the opponents.

3.2.4 According to established case law, the burden of proof rests on the patent proprietor to provide evidence capable of demonstrating the technical effect relied upon for the formulation of the objective technical problem (Case Law of the Boards of Appeal, *supra*, I.D.4.3.1). Comparative tests relied upon to demonstrate an improvement must be reproducible on the basis of the information provided and must enable the skilled person to verify the relevance of the results (Case Law of the Boards of Appeal, 11th ed. 2025 I.D. 4.3.2).

3.2.5 The experimental data of 2019 lack essential information regarding the experimental set-up. In particular, the compositions tested, the concentrations of the active agents, the presence and amounts of excipients, and the number and characteristics of the test animals are not disclosed. In the absence of such information, it cannot be ascertained whether comparable conditions were applied or whether the reported results are statistically meaningful. The relevance of the data for demonstrating an improvement over the closest prior art is therefore not verifiable.

Furthermore, the results themselves do not appear to demonstrate a consistent improvement of the dimesylate salt over the dihydrochloride. Figure 2 shows varying relative effects over the three days of administration, with the dihydrochloride exhibiting an apparent greater reduction in IOP after administration on day 1, the dimesylate achieving a greater reduction after administration on day 2, and apparently similar levels of reduction being reached after administration on

day 3, with no clear overall superiority of the dimesylate. These data do not support the existence of a consistent advantage over the tested treatment period. In addition, the data relating to the dimesylate salt are not internally consistent, since the pattern of intraocular pressure reduction by the dimesylate salt of netarsudil differs between Figures 2 and 3, although these figures relate to experiments of the same type. No explanation is provided for these discrepancies.

The Board also notes that the experimental period is limited to three days. In view of the observed variability of the results, this short observation period does not permit a reliable assessment of a consistent therapeutic advantage.

3.2.6 The proprietor's argument that the skilled person could derive the relevant experimental conditions from common general knowledge, in particular general familiarity with rabbit IOP models, or from Example 9 of the patent, does not overcome these deficiencies. The absence of essential parameters prevents verification of the results. This is not remedied by reference to Example 9, which concerns a specific formulation comprising a combination with latanoprost, whereas the experimental data of 2019 do not establish that comparable conditions, in particular a combined formulation, were applied.

Nor is the absence of counter-evidence decisive. Where the party bearing the burden of proof has not provided sufficiently reliable and verifiable evidence of the alleged effect, the lack of opposing experimental data cannot remedy that deficiency.

The case law cited by the proprietor (T 536/07; T 184/16) concerns situations in which there was no *prima facie* reason to doubt that the claimed effect could be achieved and in which post-published evidence credibly demonstrated that effect (see T 536/07, Reasons 8-11 and 20-24; T 184/16, Reasons 7.2). The present case differs in that the existence of the alleged improvement is not convincingly established by the evidence on file.

3.2.7 For these reasons, the Board concludes that the supplemental experimental data filed on 3 October 2019 do not convincingly demonstrate an improvement of the dimesylate salt of netarsudil over the dihydrochloride disclosed in document D6.

Accordingly, for the purpose of assessing the inventive step of claim 1, the objective technical problem is formulated as the provision of an alternative salt form of the netarsudil compound and corresponding compositions comprising such a salt.

3.3 Assessment of the solution

3.3.1 Documents D12, D14, D30 and D31 describe the selection of pharmaceutically acceptable salts as a routine step in drug development and identify mesylate salts among the commonly used acid addition salts of basic active pharmaceutical ingredients (see e.g. D12, page 3; D14, Table I; D30, page 1418, Table II; D31, page 2950, Table I). These documents show that mesylates belong to the standard set of salts considered by the skilled person when selecting a suitable salt form.

3.3.2 The patent proprietor argued, with reference to document D7, that hydrochloride salts are by far the

most frequently used salts and that mesylates are not commonly employed, such that the skilled person would have had no reason to select the dimesylate. However, Table 2 of document D7 (page 6667) shows that, although hydrochlorides represent the largest proportion (above 50%), mesylate salts still account for approximately 4% of the acid addition salts and therefore form part of the commonly used alternatives.

3.3.3 In a situation where the objective technical problem is the provision of an alternative, the selection of one among a number of known and commonly used options is obvious and does not require any specific pointer in the prior art (Case Law of the Boards of Appeal, *supra*, I.D.9.21.9).

3.3.4 Starting from the dihydrochloride salts of netarsudil in its racemic or enantiomeric forms disclosed in document D6, the skilled person would therefore have considered the preparation of the mesylate salts as defined in claims 8-10 to be an obvious alternative.

3.3.5 As set out in section 3.1 above, the subject-matter of claims 1-7 and 11-12 additionally differs from the teaching in document D6 by the combination of the dimesylate salt of the netarsudil compound with a prostaglandin compound selected from the defined group.

3.3.6 Document D6 itself already discloses the combination of Rho kinase inhibitors, including netarsudil, with prostaglandin compounds such as latanoprost (see document D6, column 17, line 55 to column 18, line 8). The skilled person is thus directly taught to combine the netarsudil compound in its racemic or enantiomeric forms, including salts thereof, with a prostaglandin compound.

This teaching is corroborated by documents D2, D21 and D32, which describe that the combination of a Rho kinase inhibitor with a prostaglandin analog results in an enhanced reduction of intraocular pressure (see e.g. document D2, paragraphs [0005]-[0008]; document D21, paragraphs [0010]-[0013]; document D32, page 2, left column). These documents confirm that such combinations form part of the common general approach to improving IOP reduction.

In the absence of any technical effect associated with the specific choice of the salt, the skilled person, starting from document D6 and seeking to provide an alternative, would have applied this teaching to the dimesylate salt and combined it with a prostaglandin as defined in claim 1.

No evidence has been provided for any effect associated with the claimed combination beyond the known effect of such combinations in the prior art.

Accordingly, the subject-matter of claim 1 does not involve an inventive step.

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 A. Usuelli

Decision electronically authenticated