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Datasheet for the decision of 30 January 2023

Case Number: T 1065/18 - 3.3.02

Application Number: 10167344.0

Publication Number: 2399911

IPC: C07D277/56, A61K31/425, A61P19/06

Language of the proceedings: EN

Title of invention:
Polymorphs of Febuxostat

Patent Proprietor:
SANDOZ AG

Opponents:
Alfred E. Tiefenbacher (GmbH & Co. KG)
Teva Pharmaceutical Industries Ltd

Relevant legal provisions:
EPC Art. 84, 56
EPC R. 103(1)(a)
RPBA Art. 12(4)
RPBA 2020 Art. 13(2)

Keyword:

Clarity
Inventive step - try and see situation, bonus effect
Reimbursement of appeal fee
Substantial procedural violation - appealed decision reasoned
Late-filed evidence - submitted with the statement of grounds of appeal - submitted shortly before oral proceedings

Decisions cited:

G 0003/14, T 0595/90, T 0352/04, T 0205/14, T 1667/15, T 1598/18, T 2604/18, T 2295/19

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Case Number: T 1065/18 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 30 January 2023

Appellant: (Patent Proprietor)	SANDOZ AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Prüfer & Partner mbB Patentanwälte · Rechtsanwälte Sohnckestraße 12 81479 München (DE)
Appellant: (Opponent 1)	Alfred E. Tiefenbacher (GmbH & Co. KG) Van-der-Smissen-Straße 1 22767 Hamburg (DE)
Representative:	Hamm&Wittkopp Patentanwälte PartmbB Jungfernstieg 38 20354 Hamburg (DE)
Appellant: (Opponent 2)	Teva Pharmaceutical Industries Ltd 124 Dvora HaNevi'a St. 6944020 Tel Aviv (IL)
Representative:	Eder, Michael Df-mp Dörries Frank-Molnia & Pohlman Patentanwälte Rechtsanwälte PartG mbB Fünf Höfe Theatinerstrasse 16 80333 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 26 March 2018 concerning maintenance of the European Patent No. 2399911 in amended form.**

Composition of the Board:

Chairman	M. O. Müller
Members:	A. Lenzen
	L. Bühler

Summary of Facts and Submissions

I. The present decision concerns the appeals filed by the patent proprietor, opponent 1 and opponent 2 against the decision of the opposition division (decision under appeal) according to which European patent No. 2 399 911 (patent) in amended form meets the requirements of the EPC.

Since all parties are both appellants and respondents at the same time, the board will continue to refer to them as the patent proprietor, opponent 1 and opponent 2 (or to the latter two jointly as the opponents) for the sake of simplicity.

II. The following documents submitted before the opposition division are relevant to the present decision:

D2 US 7,361,676 B2
D3 WO 2010/144685 A1
D9 Yu, L. X., Pharmaceutical Research 2003, vol. 20, No. 4, pages 531 to 536
D11 Brittain, H. G., "Polymorphism in Pharmaceutical Solids", New York: Marcel Dekker, Inc., 1999, pages 1 to 33 and 183 to 226
D17 Caira, M. R., "Crystalline Polymorphism of Organic Compounds", Topics in Current Chemistry, vol. 198, Springer, 1998, pages 163 to 208
D20 "Annex 2", comprising experiments 1 and 2 (2 pages)
D27 Giron, D., Thermochimica Acta 1995, vol. 248, pages 1 to 59
D28 "Febuxostat - Preparative DSC & Temperature dependent XRPD studies" (8 pages)
D31 "DSC of form A of Febuxostat (aetFEB019EXP002)

disclosed in HW 15" (1 page)

III. With the statement of grounds of appeal, the patent proprietor filed the sets of claims of the main request and auxiliary requests 1 to 18. It also filed three documents concerning the Karl Fischer method for determining the water content of a sample, with which it intended to counter the opposition division's clarity objections raised in this respect against claim 1 of the (then and present) main request. As the clarity objection addressed in the present decision is different from that discussed before the opposition division, the three aforementioned documents are not relevant.

IV. With the statements of grounds of appeal, the opponents filed, *inter alia*, the following documents:

A37 Highlights of prescribing information, ULORIC (febuxostat) tablet for oral use (17 pages)
A38 Threlfall, T. L., Analyst 1995, vol. 120, pages 2435 to 2460
A39 Burger, A., Pharmazie in unserer Zeit 1982, vol. 11, No. 6, pages 177 to 189
A40 "HW 20" (DSC of form A; one page)

V. With the reply to the opponents' statements of grounds of appeal, the patent proprietor filed the set of claims of auxiliary request 19 and the following document:

A44 "D45" (DSC of form A at different heating rates and weights; one page; this document had already been filed before the opposition division)

It also filed two further documents as evidence that the improved solubility of febuxostat form I as described in the patent compared to febuxostat form A of D2 was relevant and should be taken into account. Since the board could not acknowledge an inventive step, even if taking into account the alleged improvement and formulating the objective technical problem more ambitiously, as proposed by the patent proprietor, these documents turned out not to be relevant to the present decision.

VI. With its letter dated 16 April 2019, opponent 1 filed, *inter alia*, the following document:

A45 Neuenfeld, S., "Polymorphieuntersuchungen von Pharmawirkstoffen mittels Thermischer Analyse", Anwenderseminar Thermische Analyse: Würzburger Tage 1998, 1st edn, 1999, pages 92 to 115

VII. In preparation for the oral proceedings, arranged at the parties' request, the board issued a communication pursuant to Article 15(1) RPBA 2020.

VIII. With its letter dated 25 January 2023, the patent proprietor filed the following document:

A47 Kitamura, M., Crystal Growth & Design 2004, vol. 4, No. 6, pages 1153 to 1159

IX. The oral proceedings before the board took place as a videoconference on 30 January 2023 in the presence of all parties. The board decided to admit auxiliary request 4 and A40 but not to admit A47. The board also decided to reject opponent 1's request for reimbursement of the appeal fee. At the end of the oral

proceedings, the chair announced the order of the present decision.

X. Summaries of the patent proprietor's arguments relating to the admittance of A40 and A47 and to the allowability of the main request and auxiliary requests 1 to 19 are contained in the reasons for the decision.

XI. The opponents' arguments relating to the admittance of A40 and A47 and to the allowability of the main request and auxiliary requests 1 to 19 can be summarised as follows.

- Admittance of A40 and A47

  A40 was filed together with A38 and A39 in a reaction to the opposition division's reasoning in the decision under appeal. A40 should be admitted.

  A47 was a reaction to A40. It should have been filed with the patent proprietor's reply to the opponents' statements of grounds of appeal. However, it should not have been filed only very shortly before the oral proceedings before the bord. Contrary to Article 13(2) RPBA 2020, there were no exceptional circumstances that could justify the late filing of A47.

- Main request and auxiliary request 1

  The board's preliminary view in its communication pursuant to Article 15(1) RPBA 2020 was correct. Claim 1 of the main request lacked clarity. The same applied to claim 1 of auxiliary request 1.

- Auxiliary requests 2 and 3

  Claim 1 of auxiliary requests 2 and 3 lacked clarity. The reasoning of T 352/04 (point 2.8 of the Reasons) applied *mutatis mutandis*.

- Auxiliary request 4

  D2 was the closest prior art and febuxostat form A disclosed therein was the most suitable starting point for the assessment of inventive step. The subject-matter of claim 1 differed from form A in that it related to form I instead of form A and in that form I was comprised in a pharmaceutical composition in oral dosage form.

  The higher solubility of form I compared to that of form A was only marginal and had no relevance for a therapeutic application. Furthermore, the solubility tests in the patent were conducted with a mixture of methanol and water. No conclusions concerning a biological system could be drawn from these solubility tests. Therefore, this effect should not be taken into account for the objective technical problem.

  The patent, in particular figure 8, could not provide any information about the intrinsic dissolution rates of forms I and A. This was because the patent did not contain any data relating to the surface area of the samples used for solubility testing.

  There was no comparison of forms I and A in terms of hygroscopicity. Therefore, even if form I was

non-hygroscopic, this should not be taken into account for the objective technical problem.

The board rightly considered that the question of whether form I could be reliably obtained in a stable, robust and repeatable manner did not relate to form I itself but to a process for its manufacture. This should, likewise, not be taken into account for the objective technical problem.

Hence, the objective technical problem was to provide a pharmaceutical composition in oral dosage form comprising an alternative crystalline form of febuxostat. Even if the objective technical problem had been formulated in more ambitious terms taking into account the higher solubility of form I compared to form A, the solution would have been obvious. This was because the relevant common general knowledge, more specifically the heat-of-transition rule, would have urged the skilled person to look for forms resulting from form A by an endothermic phase transition at higher temperatures. The experimental evidence in the present case showed that, by proceeding in that way, the skilled person would have routinely found form I. Moreover, the solution to the objective technical problem would still have been obvious even if the non-hygroscopicity of form I had been taken into account. The fact that form I retained the non-hygroscopicity of form A was merely a bonus effect that the skilled person, who was primarily looking for a new crystalline solid form of febuxostat with higher solubility, would inevitably have achieved. Finally, the provision of an oral dosage form of a solid form which was not inventive was not based on an inventive step either.

Thus claim 1 of auxiliary request 4 did not involve an inventive step.

- Auxiliary requests 5 to 19

As correctly pointed out by the board, the additional features in claim 1 of auxiliary requests 5 to 19 could not confer an inventive step either. Hence, the subject-matter of claim 1 of each of auxiliary requests 5 to 19 did not involve an inventive step.

Summaries of opponent 1's arguments relating to its request for reimbursement of the appeal fee are contained in the reasons for the decision.

XII. The parties' final requests relevant to the present decision were as follows.

The patent proprietor requested

- that the decision under appeal be set aside and that the patent be maintained in amended form based on one of the sets of claims of the main request or auxiliary requests 1 to 18, filed with the statement of grounds of appeal, or auxiliary request 19 filed with the reply to the opponents' statements of grounds of appeal
- that A37 and A40 not be admitted.

Opponents 1 and 2 requested

- that the decision under appeal be set aside and the patent be revoked in its entirety
- that A47 and auxiliary request 4 not be admitted.

Opponent 1 also requested that the appeal fee be reimbursed.

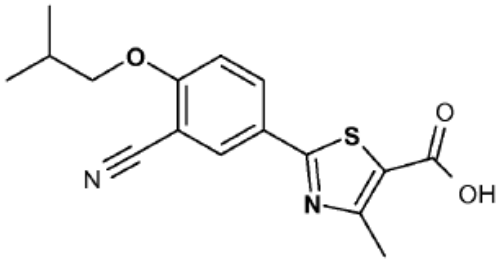
Reasons for the Decision

Main request - Clarity (Article 84 EPC)

1. Claim 1 reads as follows (amendments shown vis-à-vis claim 1 as granted):

> "*Crystalline form of Febuxostat having an X-ray powder diffraction pattern as measured using CuK$\alpha_{1,2}$ radiation having a wavelength of 0.15419 nm comprising peaks at 2-theta angles of 6.6 ± 0.2°, 12.8 ± 0.2°, 24.5 ± 0.2°, 25.8 ± 0.2°, 26.6 ± 0.2° and being characterized by an IR spectrum comprising absorption bands at wavenumbers of 2960 ± 2 cm^{-1}, 2874 ± 2 cm^{-1}, 2535 ± 2 cm^{-1}, 2229 ± 2 cm^{-1}, 1673 ± 2 cm^{-1}, 1605 ± 2 cm^{-1}, 1509 ± 2 cm^{-1}, 1422 ± 2 cm^{-1}, 1368 ± 2 cm^{-1}, 1323 ± 2 cm^{-1}, 1274 ± 2 cm^{-1}, 1166 ± 2 cm^{-1}, 1116 ± 2 cm^{-1}, 1045 ± 2 cm^{-1}, 1013 ± 2 cm^{-1}, 911 ± 2 cm^{-1}, 820 ± 2 cm^{-1}, 763 ± 2 cm^{-1} and 725 ± 2 cm^{-1} when measured using a diamond attenuated total reflection (ATR) cell,* ***further characterized as being an anhydrous form having a water content, when stored at 20°C at ambient pressure in an environment from 0% up to 90% relative humidity, of below 0.1 % according to Karl Fischer (KF).***"

2. The compound referred to in claim 1, febuxostat, is a medicament used in the treatment of hyperuricemia and gout. It has the following structure (patent, paragraph [0002]):



The crystalline form of febuxostat defined in claim 1 on the basis of 2-theta angles and wavenumbers is referred to in the patent as "form I" (patent, paragraph [0015]).

3. The feature distinguishing claim 1 of the main request from the granted claim 1 (in bold above) is not contained in the granted claims. Hence, with respect to this additional feature, claim 1 of the main request is open to an assessment under Article 84 EPC (G 3/14, OJ EPO 2015, A102, Order).

3.1 The patent proprietor argued that the additional feature should be interpreted as meaning that form I had to have a water content of below 0.1% according to Karl Fischer (KF) both at the beginning and at the end of the storage period.

3.2 The board cannot agree with this construction. As far as the additional feature can be understood, it defines form I as having a water content of below 0.1% according to KF after storage under certain conditions. This means that the water content after storage can in fact be different from that before storage.

The storage conditions of claim 1 cover any storage time and a relative humidity during storage ranging from as low as 0% to as high as 90%. Storage of a

water-containing crystal form for a sufficiently long period of time at a sufficiently low relative humidity, results in water loss. Claim 1, therefore, covers crystal forms with an initial water content of 0.1% or more which lose such an amount of water during storage at very low relative humidity over a very long period of time that the resulting final water content is below 0.1%, as required by claim 1.

Furthermore, the relative humidity during storage is not limited in claim 1 to a low relative humidity. Instead, it may be as high as 90%. Any crystal form described in the preceding paragraph, i.e. a crystal form having an initial water content of 0.1% or more before storage and a water content according to claim 1 after storage for a sufficiently long period of time at a sufficiently low relative humidity, may lose less water - or no water - if stored at a high relative humidity, with the result that its final water content after storage is greater than 0.1%.

Thus, depending on the relative humidity during storage, the same crystal form may or may not be according to claim 1 with respect to its water content after storage. For this reason claim 1 of the main request lacks clarity. The main request is not allowable.

Auxiliary request 1 - Clarity (Article 84 EPC)

4. Claim 1 of auxiliary request 1 contains the same additional feature objected to above under Article 84 EPC with respect to claim 1 of the main request. Therefore, claim 1 of auxiliary request 1 lacks clarity for the same reasons. Auxiliary request 1 is not allowable.

Auxiliary request 2 - Clarity (Article 84 EPC)

5. Claim 1 of auxiliary request 2 reads as follows (the definition of form I in terms of 2-theta angles and wavenumbers is the same as in claim 1 of the main request and has been omitted for the sake of brevity):

> "*Pharmaceutical composition comprising a crystalline form of Febuxostat ..., wherein the pharmaceutical composition is packaged or filled into a container.*"

6. The feature according to which the pharmaceutical composition "*is packaged or filled into a container*" is not contained in the granted claims. Hence, with respect to this additional feature, claim 1 of auxiliary request 2 is open to an assessment under Article 84 EPC (G 3/14, OJ EPO 2015, A102, Order).

6.1 The patent proprietor essentially argued that the claimed subject-matter arose from the claim features in their entirety. Claim 1 could not therefore be understood in any other way than as being directed to a pharmaceutical composition in a container, i.e. to a container comprising a pharmaceutical composition.

6.2 Although the claim features in their entirety define the claimed subject-matter, a claim may nevertheless be unclear. In the board's view, this is the case here. Due to its wording ("*Pharmaceutical composition ... packed or filled into a container.*"), claim 1 puts the emphasis on a pharmaceutical composition rather than a container comprising said composition. This makes it unclear whether the protection sought is limited to the pharmaceutical composition *per se*, or whether a

container comprising a pharmaceutical composition is to be protected (see T 352/04, point 2.8 of the Reasons for a similar case).

Thus, claim 1 of auxiliary request 2 lacks clarity. Auxiliary request 2 is not allowable.

Auxiliary request 3 - Clarity (Article 84 EPC)

7. With respect to the arrangement of the pharmaceutical composition and the container, claim 1 of auxiliary request 3 is worded in the same way as claim 1 of auxiliary request 2 ("*Pharmaceutical composition ... packed or filled into a container.*"). The above clarity objection therefore also applies to claim 1 of auxiliary request 3. Auxiliary request 3 is not allowable.

Auxiliary request 4 - Admittance

8. The set of claims of auxiliary request 4 was filed with the patent proprietor's statement of grounds of appeal. Both opponents requested that auxiliary request 4 not be admitted. The board decided to admit auxiliary request 4. As this request was ultimately not allowable and the opponents were therefore not adversely affected, it is not necessary to give reasons for this decision.

Auxiliary request 4 - Inventive step (Article 56 EPC)

9. Claim 1 reads as follows (the definition of form I in terms of 2-theta angles and wavenumbers is the same as in claim 1 of the main request and has been omitted for the sake of brevity):

"*Pharmaceutical composition comprising a crystalline form of Febuxostat ..., wherein the pharmaceutical composition is an oral dosage form.*"

Thus, claim 1 is directed to a pharmaceutical composition in an oral dosage form comprising form I.

10. Closest prior art and starting point

10.1 It was common ground between the parties that D2 is the closest prior art. The board saw no reason to deviate from this unanimous view.

10.2 D2 relates to solid forms of febuxostat, referred to as crystalline forms A, B, C, D and G, and as amorphous form E.

Among the crystalline forms, form A has the highest intrinsic dissolution rate (D2, column 6, reference example 2). Only form A proved stable when tablets were produced by wet granulation, while the other forms that were tested partially converted to other solid forms (columns 7 and 8). Lastly, the dissolution profiles of tablets containing form A did not change significantly after storage for 6 months at 40 °C/75% relative humidity (column 9, example 3). Thus, it can be concluded that form A is clearly the preferred form among those tested in D2, a fact which - incidentally - is also reflected in the claims of D2 as they relate only to this form.

Against this background, form A of D2 is a realistic starting point for the assessment of inventive step.

10.3 The patent proprietor argued "*that the crystalline from A of D2 specifically is not necessarily the "closest prior art".*" (reply to the opponents' statements of grounds of appeal, point 4.2). The most common approach to screening and providing new solid forms was based on crystallisation from a solution. This approach, however, entailed the loss of the crystal structure of the initial solid form. Therefore, form A was, objectively, not closer to a new solid form than any other form of febuxostat. This showed that starting from form A of D2 was based on hindsight.

As explained above, form A is singled out as clearly preferred among the solid forms of febuxostat disclosed in D2, in particular because it is the most suitable for the preparation of pharmaceutical formulations. This is the same context as that in which form I is also praised in the patent, namely as a solid form of febuxostat and in relation to its application for the preparation of pharmaceutical formulations. Contrary to the patent proprietor’s argument, form A is therefore very much a possible starting point for assessing inventive step. In the board's view, the fact that the crystal structure of an initial solid form is lost when an attempt is made to crystallise it from a solution to thereby obtain a solid form with a different crystal structure is also not a sufficient reason not to start from a specific solid form within the framework of the problem-solution approach. If one were to follow the patent proprietor's line of reasoning in this regard, any new solid form would ultimately also be inventive. The fact that the crystal structure of an initial solid form is lost in crystallisation attempts from a solution is, in any case, not relevant in the present case, since the relevant common general knowledge does not guide the skilled person to undertake such

crystallisation attempts, but to search for a new solid form in a different way, namely by thermal treatment (see below).

11. Distinguishing features

The subject-matter of claim 1 is distinguished from form A of D2 in that

- it relates to a pharmaceutical composition in oral dosage form
- the pharmaceutical composition comprises form I rather than form A.

12. Technical effects and objective technical problem

12.1 At the oral proceedings before the board, the patent proprietor formulated the objective technical problem as providing a pharmaceutical composition containing a crystalline form of febuxostat which is not hygroscopic, which has a higher solubility and intrinsic dissolution rate and which can be obtained in a stable, robust and repeatable manner. The technical effects relied on by the patent proprietor at the oral proceedings in this respect are assessed below.

In writing, the patent proprietor had also referred to other technical effects such as the high-temperature stability of form I and its storage stability (also referred to by the patent proprietor as kinetic stability). The board commented on these effects in its communication under Article 15(1) RPBA 2020. At the oral proceedings, the patent proprietor no longer relied on these technical effects when formulating the objective technical problem.

12.2 Non-hygroscopicity

The patent shows that form I is virtually non-hygroscopic and is therefore very suitable for use in a wet granulation process for the production of pharmaceutical compositions comprising febuxostat (paragraph [0022], figure 3).

As set out above, form A is also stable during a wet granulation process. It can be concluded from this that form A is also virtually non-hygroscopic. Although the patent does not directly compare forms I and A in terms of hygroscopicity and does not therefore show that form I is any better than form A in this respect, this does not mean that the non-hygroscopicity of form I must - as argued by the opponents - simply be disregarded. Therefore, this effect is taken into account.

12.3 Higher solubility

The patent (paragraphs [0020] and [0064], figure 8) compares forms I and A with regard to their solubility in MeOH/H_2O (1:1 v/v) at ambient temperature. The diagram in figure 8, in which the concentration (in mg/mL) is plotted against time (in min), shows that form I has a solubility at ambient temperature that is approximately 20% higher than that of form A in the state of equilibrium.

Without prejudice to the opponents' criticism of this data, the board assumed - for the sake of argument - in favour of the patent proprietor that the effect of a higher solubility could be considered when formulating the objective technical problem.

12.4 Higher intrinsic dissolution rate

According to the patent proprietor, figure 8 of the patent also allowed it to be concluded that form I had a higher intrinsic dissolution rate than form A. This was because the straight line connecting the origin and the first data point had a greater slope for form I than for form A.

The intrinsic dissolution rate measures the amount of substance that goes into solution per unit of area and time. It is given, for example, in the unit $mg/cm^2/min$ (see D2, reference example 2). However, the surface areas of forms A and I that were used in the solubility tests are not clear from the patent. For this reason alone, no intrinsic dissolution rates can be derived from the data given in the patent, either directly or indirectly, for example, from the diagram in figure 8.

The fact that there is no information on the intrinsic dissolution rates also distinguishes the present case from that underlying decision T 1667/15 (see point 3.1.8 of the Reasons), on which the patent proprietor relied in support of inventive step. That case is therefore not relevant to the present case.

12.5 Process-related effects

The patent proprietor also argued that the way in which form A was obtained in D2 was associated with a number of drawbacks. These included, e.g., the crystallisation conditions having to be carefully controlled in order to obtain polymorphically pure form A. In contrast, form I could be reliably obtained in a stable, robust and repeatable manner.

The advantages relied on by the patent proprietor might be relevant to a process for making form I, but they are not relevant to form I as such (see T 205/14, point 5.6.4 of the Reasons for a similar case). This is because they are ultimately not based on a comparison of forms I and A but on a comparison of the processes for making those forms.

12.6 Hence, from the effects relied upon by the patent proprietor, only the non-hygroscopicity and - for the sake of argument - also the higher solubility can be taken into account.

The objective technical problem can therefore be formulated as providing a pharmaceutical composition containing a crystalline form of febuxostat which is non-hygroscopic and has higher solubility.

13. Obviousness

13.1 With regard to the assessment of obviousness, the board considers it appropriate to first summarise the following aspects concerning polymorphs relevant to the present decision (for useful overviews: D9, page 532, right column, second paragraph; D11, chapter III on page 18 f. and table 4; D17, paragraph bridging pages 166 and 167; D27, pages 11 ff.; A38, pages 2437 f. and 2446 to 2449; A39, pages 186 to 188; A45, pages 97 ff.). There was agreement between the parties that these aspects belong to the skilled person's common general knowledge.

- The transition between two polymorphs can be categorised as either enantiotropic or monotropic.
- In a monotropic system, the higher-melting polymorph is always (thermodynamically) more stable

than the lower-melting polymorph. The transition from the lower-melting to the higher-melting polymorph is thus irreversible.

- In an enantiotropic system, the transition from one polymorph into another, which occurs at a certain transition temperature, is reversible. Above the transition temperature, the higher-melting polymorph is (thermodynamically) more stable, whereas below the transition temperature it is the lower melting polymorph that is more stable. As a lower (thermodynamic) stability goes hand in hand with a higher (thermodynamic) solubility, the higher-melting polymorph will have a higher solubility below the transition temperature than the lower-melting polymorph.
- The four thermodynamic rules developed by Burger and Ramberger can help decide whether two polymorphs are enantiotropes or monotropes. The most useful and applicable of these four rules are the heat-of-transition rule and the heat-of-fusion rule. The heat-of-transition rule states that, if an endothermic (exothermic) polymorphic transition is observed, the two forms are enantiotropes (monotropes). The heat-of-fusion rule states that, if the higher melting polymorph has the lower (higher) heat of fusion, the two forms are enantiotropes (monotropes).

13.2 Against the background of this common general knowledge, the skilled person, faced with the problem of providing a crystalline form of febuxostat that has a higher solubility than form A, will clearly be inclined to check whether form A undergoes an endothermic phase transition into a new higher-melting form at higher temperatures. This is because, according to the heat-of-transition rule, such a new solid form

should then be an enantiotrope of form A having a higher solubility than form A below the transition temperature, such as at ambient temperature in the present case (see point 12.3 above).

Either such a form exists or it does not. The board concurs with opponent 1 that the skilled person would have been in a "try and see" situation.

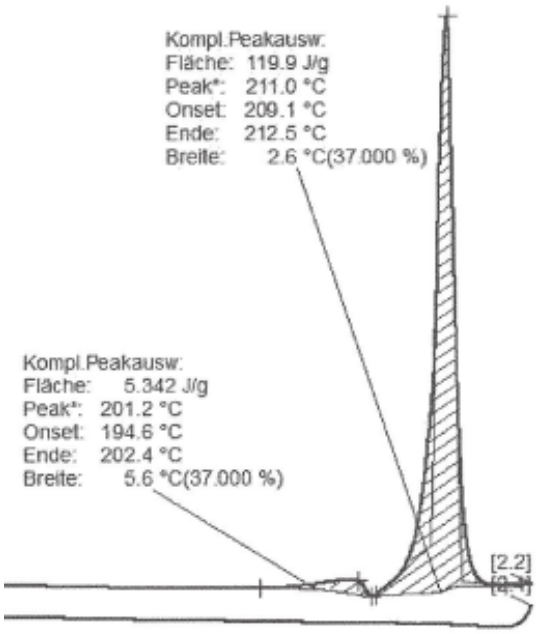
It may be true that the skilled person - as argued by the patent proprietor - does not generally think of using DSC to find new solid forms. However, against the background of the common general knowledge summarised above and the objective technical problem, they would most certainly have done so - if only because DSC measures heat flow and is the method of choice for determining exo- and endothermic processes when heating a sample.

13.3 It was a matter of dispute between the parties whether the skilled person would have found that form A undergoes an endothermic phase transition to a new solid form during a DSC analysis. To this end, opponent 1 (D28, A40) and the patent proprietor (D31, A44, A47) relied on various experimental data, the admittance of which (A40, A47) was partly contested by the other party.

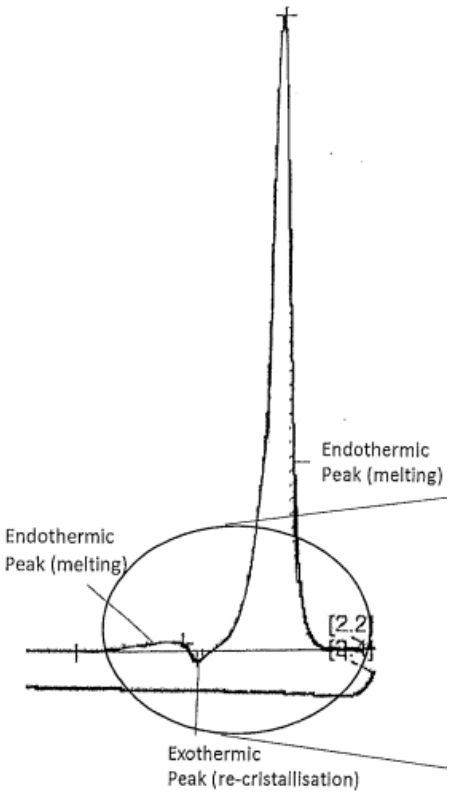
Therefore, before clarifying the question of what information the skilled person would have derived from a DSC analysis of form A, the question of admittance of A40 and A47 must first be answered.

13.4 Admittance of A40 and A47

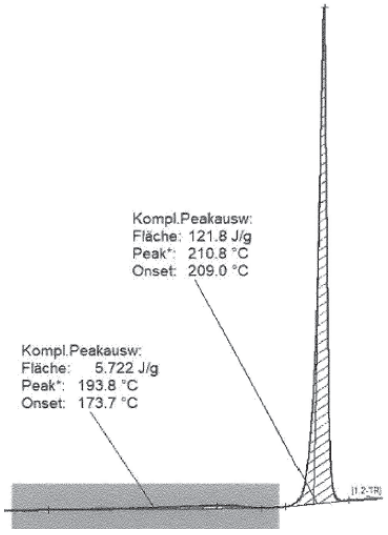
13.4.1 For the admittance of A40 and A47, the history of the case is relevant. It can be summarised as follows, with reference to the following DSC curves of form A in the various documents:



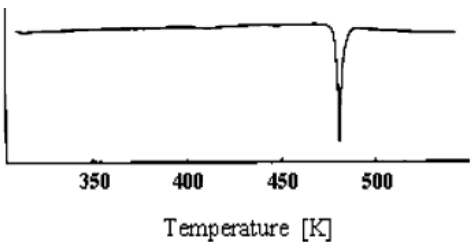
DSC of form A in D28



DSC of form A in D31



DSC of form A in A40



DSC of form A in A47

In the following paragraphs, peaks signifying an exo-/endothermic event in the DSC curve are referred to as exo-/endothermic peaks for the sake of simplicity. In the DSC curves in D28, D31 and A40, endothermic peaks point upwards, exothermic peaks downwards. In A47, it is the other way round. DSC peaks are counted in the direction of increasing temperature, i.e. from left to right.

- D28 was filed by opponent 1 during written opposition proceedings and shows a DSC curve of form A at a heating rate of 10 °C/min. According to opponent 1, this DSC curve had to be interpreted as showing two endothermic peaks, the first one corresponding to a transition of form A to a new form, the second one corresponding to the melting of the new form. Therefore, this DSC curve showed that form A and the new form were enantiotropes.
- At the oral proceedings before the opposition division, the patent proprietor filed D31. It shows an enlargement of the DSC curve in D28 with a straight base line. The patent proprietor argued that the interpretation of the DSC curve of D28 had to be based on that straight base line. This showed an exothermic peak between two endothermic peaks. This peak sequence did not obviously show enantiotropy as it could also be due to a monotropic phase transition.
- In the decision under appeal, the opposition division accepted the patent proprietor's interpretation of D28 as shown in D31 and ultimately acknowledged an inventive step.
- A40 was filed by opponent 1 with the statement of grounds of appeal. It shows a DSC curve of form A at a lower heating rate (5 °C/min) than that in D28

(10 °C/min). According to opponent 1, reducing the heating rate made the exothermic peak - if it existed at all - disappear. This was explained in A38 and A39, and the DSC curve in A40 clearly showed an endothermic phase transition from form A to a new form.

- With the letter dated 25 January 2023, which was more than 4 years after opponent 1's statement of grounds of appeal, the patent proprietor filed A47. It shows a DSC curve of form A at a heating rate of 5 °C/min. Unlike the DSC in A40, the one in A47 only shows one endothermic peak.

13.4.2 As regards the admittance of A40 and A47, the patent proprietor essentially argued that A47 showed an unbiased DSC analysis of form A. This DSC analysis was highly relevant. Although the heating rate was the same as in A40 (5 °C/min), the DSC curve showed only one endothermic peak. Thus, a normal DSC analysis would not have indicated or hinted in any way at a thermal transition of form A to a new form. The interpretation of A47 did not pose any difficulties. A47 was also filed in response to the the board's communication pursuant to Article 15(1) RPBA 2020, which highlighted the importance of the experimental evidence in relation to the DSC analyses submitted to that date. Hence, A47 should be admitted. This would apply all the more in the event of A40 being admitted, as this document had also been submitted late.

13.4.3 The board's position is as follows.

(a) The filing of opponent 1's document A40 together with A38 and A39 constitutes an appropriate response to the developments before the opposition division, more specifically to the opposition

division's reasoning based on D31 in the decision under appeal. Assuming the correctness of the patent proprietor's interpretation of D28 in D31, A38 (page 2447, right column, second paragraph and figure 6) and A39 (page 188, left column, penultimate paragraph and figure 11) show a possible cause for the sequence of endo-, exo- and endothermic peaks allegedly observed in D28. At the same time, A38 and A39 show a possible way of clarifying the matter, namely reducing the heating rate and this is exactly what opponent 1 did in A40. Compared to the measurement in D28, the heating rate was halved in A40 from 10 to 5 °C/min. A40 was filed together with opponent 1's statement of grounds of appeal, i.e. at the earliest stage on appeal. As D31 was not filed by the patent proprietor until the oral proceedings before the opposition division, opponent 1's filing of A40 could not have been expected at an earlier stage either.

At the oral proceedings, therefore, the board decided to admit A40 (Article 12(4) RPBA 2007).

(b) The filing of A47 constitutes an amendment of the patent proprietor's appeal case. A47 was filed with the patent proprietor's letter dated 25 January 2023. This was after notification of the summons to oral proceedings. Pursuant to Article 13(2) RPBA 2020, A47 is not to be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the patent proprietor. However, in the present case, there are no such exceptional circumstances. The late filing of A47 cannot be excused by it being filed in response to the

board's communication under Article 15(1) RPBA 2020. This is because the board's communication was only based on the parties' earlier submissions and did not raise any new issues. Furthermore, even if one were to acknowledge that A47 is *prima facie* relevant, this would not constitute an exceptional circumstance within the meaning of Article 13(2) RPBA 2020.

The patent proprietor argued that a merely formalistic approach to admittance, thereby disregarding the relevance of the submission, was not appropriate. However, the relevance of a submission cannot be the overriding consideration for admittance irrespective of the stage of that submission. Indeed, if late-filed submissions were admitted for their relevance no matter what stage the procedure had reached and whatever the reasons for late submission, this would not only reward negligence but would also invite tactical abuse. Moreover, the board did not adopt a merely formalistic approach, but did in fact consider whether the late submission of document A47 was detrimental to procedural economy or adversely affected the other party (see decision T 1598/18, point 25.1 of the Reasons, T 2295/19, point 3.4.12 of the Reasons, T 2604/18, points 1.3 and 1.4 of the Reasons, holding that exceptional circumstances exist if the late submission does not negatively affect the other party and the efficient conduct of oral proceedings). In the present case, it is not readily apparent why two DSCs of the same solid form (form A) recorded at the same heating rate (5 °C/min) showed two different results, namely two endothermic peaks (A40) or only one (A47). The admittance of A47 would have made it necessary to

find out the reason for this discrepancy. This would have required the discussion of complex questions only at the oral proceedings, e.g. the accuracy of the DSC method in general and in the specific context of A40/A47 in relation to form A. Such complex questions had not been discussed prior to the oral proceedings before the board. Thus, A47 actually raises new issues rather than being suitable for resolving existing issues. The filing of A47 was thus prejudicial to both procedural economy and to the opponents having an opportunity to duly reply to the new submission.

At the oral proceedings, therefore, the board decided not to admit A47 (Article 13(2) RPBA 2020).

13.5 In view of the experimental evidence in the proceedings (D20, D28, D31, A40 and A44), the board came to the following conclusion as regards obviousness.

13.5.1 Even if one were to agree with the patent proprietor's interpretation of D28 in D31, namely that the DSC curve of form A in D28 is to be interpreted as a sequence of endo-, exo- and endothermic peaks and that this sequence is not unique to enantiotropic phase transitions insofar as it can also be observed in certain monotropic phase transitions, the skilled person is well aware that an enantiotropic phase transition could underlie this peak sequence. In fact, it is common for a polymorph to show a transition to a higher-melting polymorph at the appropriate transition temperature if heated slowly, but to overshoot and melt at its own melting point under more rapid heating conditions. This is often followed immediately by re-solidification to the higher-melting polymorph, thereby giving a characteristic sequence of endo-,exo- and

endothermic peaks (A38, page 2447, right column, second paragraph). In view of this, it is also clear to the skilled person that this "overshooting" may possibly be prevented by reducing the heating rate. This has been done in A40. A40 shows a DSC curve which is archetypical of an enantiotropic phase transition followed by melting of the higher-melting form, there being two endothermic peaks, the first signifying a much smaller heat transfer than the second (see, e.g., A39, page 188, figure 11). This reflects the fact that the energy difference between two solid forms of the same compound is generally much smaller than that between the solid state and the liquid (molten) state (A39, page 188, left column, penultimate paragraph).

13.5.2 In this context, the patent proprietor referred to the DSC curves of form A in A44. They showed a sequence of endo-, exo- and endothermic peaks and were recorded at heating rates (10 and 20 °C/min) and sample weights (about 1.7 and 4.5 mg) typical for such measurements. Since the use of typical heating rates and sample weights yielded DSC curves with a peak sequence that did not allow a clear conclusion to be drawn as to whether it was an enantiotropic or monotropic phase transition, the skilled person could have obtained the DSC curve shown in A40, but it could not be said that he would necessarily have obtained it if confronted with the objective technical problem.

The board does not find this convincing, for the following reasons. As already stated above, against the background of their common general knowledge the skilled person would have reduced the heating rate if in doubt about the interpretation of the DSC curve in D28. The heating rate chosen by opponent 1 in A40 in this context (5 °C/min) is by no means unusual or

unusually low. This is also illustrated by, e.g., A39, which uses heating rates as low as only 0.5 °C/min for similar investigations (figure 11). Against this background the results of A44 cannot be deemed to contradict the above conclusion - if only because they were obtained with heating rates of at least 10 °C/min, which is higher than that used in A40 (5 °C/min). To the extent that the patent proprietor's argument implies that in order to record the DSC curve in A40, the amount of form A only needed to be chosen low enough (i.e. lower than the typical amounts chosen by the patent proprietor in A44) to make the exothermic peak in the DSC disappear, it did not provide any proof for this assertion. On the contrary, the peaks of the DSC curve in A44 measured with a lower sample weight are of lower intensity than those of the DSC curve measured with a higher sample weight, but both DSC curves still show the same qualitative sequence of endo-, exo- and endothermic peaks. Hence, the results of A44 do not contradict the above conclusion for this reason either.

13.5.3 Contrary to the above, the patent proprietor still considered A40 as evidence that form A and the new form were monotropes. It argued that the first endothermic peak in A40 corresponded to the melting of the lower-melting form, the second endothermic peak to the melting of the higher-melting form. Considering the heat-of-fusion rule (see above) and the fact that the heat of fusion of the higher-melting form was higher, it had to be concluded that both forms were monotropes.

This is not convincing already on account of the patent proprietor's correlation of the first peak in the DSC curve of A40 with a melting event. As explained above, the energy difference between two solid forms of the

same compound is generally much smaller than that between the solid and liquid states. Similarly, the heats of fusion of two solid forms of the same compound having melting points close to each other should not be as different as the DSC curve in A40 suggests. Furthermore, assuming that the first endothermic peak corresponds to the melting of the lower-melting form, the DSC curve should not actually show any further melting (as attributed to the second endothermic peak) - at least not without crystallisation being observed first, which is obviously not the case with the DSC curve of A40 due to the absence of an exothermic peak.

13.5.4 Opponent 1 further showed by means of preparative DSC that heating form A up to 205 °C, i.e. to just below the melting temperature of the higher-melting form, resulted in the formation of form I (D28, pages 3 and 4). Similarly, the patent proprietor showed in D20 (example 2) that a temperature of 185 °C is already sufficient for this transformation to occur. These results are consistent with the DSC in A40 showing that the first endothermic peak spans across a temperature range of approximately 175 to 200 °C.

13.6 Thus, by performing a DSC analysis of form A, the skilled person aiming at higher solubility would have identified form I as being the desired form, i.e. a higher-melting form that results from form A by an endothermic phase transition at higher temperatures. In view of the heat-of-transition rule, they would have expected form I to be an enantiotrope of form A and form I to have a higher solubility than form A at temperatures below the transition temperature (somewhere between approx. 175 and 200 °C), i.e. at ambient temperature. Further, the fact that form I merely retains the non-hygroscopicity of form A (in the

absence of a comparison, one can, at any rate, not speak of an improvement - see above) can be considered merely as a bonus effect that the skilled person inevitably achieves because they are primarily looking for a crystalline form of febuxostat with higher solubility.

The board cannot agree with the patent proprietor's argument based on decision T 595/90 that form I was inventive already because no way of making it had been found by the effective date of the patent. Decision T 595/90 (OJ EPO 1994, 695, point 5 of the Reasons) held that "*an otherwise obvious entity, may become nevertheless non-obvious and claimable as such, if there is no known way or applicable (analogy) method in the art to make it* ***and the*** *claimed* ***methods for its preparation are therefore the first to achieve this in an inventive manner***" (emphases added). However, the present case is different in that - as explained above - the skilled person would have obtained form I in an obvious manner, i.e. the process carried out until form I is obtained is also not based on an inventive step.

Therefore, form I mentioned in claim 1 does not involve an inventive step.

The provision of a pharmaceutical composition in oral dosage form does not require inventive skills either. The patent proprietor also never argued that the opposite was the case.

13.7 It follows that the subject-matter of claim 1 of auxiliary request 4 does not involve an inventive step. Auxiliary request 4 is not allowable.

Auxiliary requests 5 to 19 - Inventive step (Article 56 EPC)

14. At the oral proceedings, the board pointed out that claim 1 of each of the auxiliary requests 5 to 19 was also based on form I, but that it could not see why any of the additional features included in claim 1 of these requests should contribute to an inventive step. The patent proprietor conceded that the answer to the question of whether the subject-matter of claim 1 of auxiliary requests 5 to 19 was based on an inventive step depended solely on whether form I was based on an inventive step.

As form I is not based on an inventive step, it must be concluded that the subject-matter of claim 1 of auxiliary requests 5 to 19 is also not based on an inventive step. Accordingly, auxiliary requests 5 to 19 are not allowable.

Reimbursement of the appeal fee

15. As summarised in the decision under appeal (page 9, paragraph 2), one of the lines of argument of opponent 1 as regards lack of sufficiency was as follows.

D3 disclosed febuxostat form F10. Form F10 was different from form I of the patent. This was because form I showed additional peaks at 2-theta angles of 7.1, 8.0 and 26.0. While both forms I and F10 fell within the scope of the claims, the patent only disclosed how form I could be obtained but not form F10. Consequently, the invention was not sufficiently disclosed.

16. According to opponent 1, the opposition division did not provide an adequate reasoning in its decision with regard to this objection. This lack of reasoning constituted a substantial procedural violation, which justified the reimbursement of the appeal fee (Rule 103(1)(a) EPC).

17. The board does not agree with opponent 1. In view of the reasoning in the decision under appeal (page 10, paragraph 2), a deciding factor for the opposition division was that the preparation of at least one solid form falling within the scope of the claims, namely form I, is disclosed in the patent. Although the opposition division does indeed appear to have actually attributed the peaks at 7.1, 8.0 and 26.0 to form F10 and not to form I - as argued by opponent 1 - it can still be concluded that the opposition division considered the disclosure of the preparation of further solid forms falling within the scope of the claims to be dispensable. The issues of whether this reasoning is convincing or erroneous and whether or not opponent 1 can agree with it have nothing to do with a lack of reasoning.

For these reasons, the board decided to reject opponent 1's request for reimbursement of the appeal fee.

Final remark

18. The patent proprietor also requested that A37 not be admitted. As this document is not relevant to the present decision, there was no need to decide on its admittance at the oral proceedings before the board.

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:

N. Maslin M. O. Müller

Decision electronically authenticated