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Datasheet for the decision of 25 January 2023

Case Number: T 1057/21 - 3.3.07

Application Number: 16188627.0

Publication Number: 3124018

IPC: A61K9/20, A61K9/28, A61K31/4196, A61P39/04

Language of the proceedings: EN

Title of invention:
ORAL FORMULATIONS OF DEFERASIROX

Patent Proprietor:
NOVARTIS AG

Opponents:
HGF Limited
Teva Pharmaceutical Industries Ltd.

Headword:
Oral Formulations of Deferasirox / NOVARTIS

Relevant legal provisions:
EPC Art. 123(2), 76(1), 123(3), 56
RPBA 2020 Art. 12(2), 12(4), 13(2)

Keyword:
Item of evidence filed after summons - admitted (yes)
Amendments - extension beyond the content of the (parent) application as filed (no) - extension of the scope of protection (no)
Inventive step - no reasonable expectation of success
Amendment to case - amendment admitted (no)

Decisions cited:
G 0005/83, T 0154/04, T 2730/16, T 0526/21

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Case Number: T 1057/21 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 25 January 2023

Appellant: (Patent Proprietor)	NOVARTIS AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Carpmaels & Ransford LLP One Southampton Row London WC1B 5HA (GB)
Appellant: (Opponent 1)	HGF Limited 1 City Walk Leeds Yorkshire LS11 9DX (GB)
Representative:	HGF HGF Limited 1 City Walk Leeds LS11 9DX (GB)
Appellant: (Opponent 2)	Teva Pharmaceutical Industries Ltd. 124 Dvora HaNevi'a St. 6944020 Tel Aviv (IL)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 27 May 2021 concerning maintenance of the European Patent No. 3124018 in amended form.**

Composition of the Board:

Chairman	A. Usuelli
Members:	J. Lécaillon
	L. Basterreix

Summary of Facts and Submissions

I. European patent 3 124 018 (hereinafter "the patent") was granted on the basis of 9 claims. The independent claim of the patent as granted read as follows:

"1. A film coated tablet for oral administration which contains deferasirox or a pharmaceutically acceptable salt thereof present in an amount of from 45% to 60% by weight based on the total weight of the tablet, and wherein the tablet contains 90 mg, 180 mg or 360 mg of deferasirox or a pharmaceutically acceptable salt thereof, wherein the tablet further comprises,
(i) at least one filler in a total amount of 10% to 40% by weight based on total weight of the tablet, wherein the filler is microcrystalline cellulose;
(ii) at least one disintegrant in a total amount of 1% to 10% by weight based on the total weight of the tablet, wherein the disintegrant is cross-linked polyvinylpyrrolidone (crospovidone);
(iii) at least one binder in a total amount of 1% to 5% by weight based on the total weight of the tablet, wherein the binder is polyvinylpyrrolidone (PVP);
(iv) optionally, at least one surfactant in a total amount of 0.0% to 2% by weight based on the total weight of the tablet, wherein the surfactant is poloxamer;
(v) at least one glidant in a total amount of 0.1% to 1% by weight based on the total weight of the tablet, wherein the glidant is colloidal silicon dioxide;
(vi) at least one lubricant in a total amount of less than 0.1 % to 2% by weight based on the total weight of the tablet, wherein the lubricant is magnesium stearate; and
(vii) a coating."

II. Two oppositions were filed against the patent on the grounds that its subject-matter lacked inventive step, it was not sufficiently disclosed and it extended beyond the content of the application and the earlier application as originally filed.

III. The opposition division took the interlocutory decision that, on the basis of the claims of auxiliary request 33 filed on 19 February 2021 as auxiliary request 35 and adapted description pages filed on 20 April 2021, the patent met the requirements of the EPC.

IV. The decision of the opposition division, posted on 27 May 2021, cited *inter alia* the following documents:

D1: WO 2007/045445 A1
D3: WO 2004/035026 A1
D7: WO 2009/067557 A1
D12: WO 2010/143006 A1
D13: Assessment report EMA/CHMP/107225/2016, published 28 January 2016
D18: Aulton, Aulton's Pharmaceutics: The Design and Manufacture of Medicines, Third Edition, 2007, 293, 296-297, 451 and 455
D22: Exjade: EPAR - Product Information Annex I published first published by European Medicines Agency on 20 August 2009
D27: EP 0 914 118 B1
D28: Eadala *et al.*, Alimentary Pharmacology and Therapeutics, Vol. 29, 2009, 677-687
D29: Rowe, Raymond C *et al.*, "Handbook of Pharmaceutical Excipients" PhP Pharmaceutical Press, 6th Edition, 2009, 506-509 and 651-653
D33: "Remington: The Science and Practice of Pharmacy", 20th Edition, 2000, chapter 45

D34: Declaration from Peter Rue dated 11 December 2020 (and CV)
D37: R. Sechaud *et al.*, International Journal of Clinical Pharmacology and Therapeutics 2008, 46(2), 102-108
D39: Allen, Jr. Loyd V. *et al.*, "Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems", 9th Edition, 2011, 128-132

V. The opposition division decided in particular as follows:

(a) The main request as well as auxiliary requests 1 to 31 did not meet the requirements of Article 123(3) EPC.
(b) Auxiliary request 32 did not fulfill the requirements of Article 76(1) EPC.
(c) Auxiliary request 33 met the requirements of Articles 76(1), 123(2), 123(3), 83, 84 and 56 EPC.

VI. The patent proprietor (appellant - patent proprietor) as well as opponent 1 (appellant - opponent 1) and opponent 2 (appellant - opponent 2) lodged an appeal against the above decision of the opposition division.

VII. With its reply to the statements setting out the grounds of appeal the appellant - patent proprietor defended its case on the basis of a main request filed during the first instance proceedings on 19 February 2021 as auxiliary request 2, and on the basis of auxiliary requests 1 to 71 submitted therewith. During oral proceedings, the appellant - patent proprietor requested auxiliary request 48, initially filed on 19 February 2021 during first instance proceedings as auxiliary request 38, to become the main request and the former main request to become auxiliary request 48.

The main request contains 4 claims. Claim 1 of the main request reads as follows:

"1. A swallowable film coated tablet which contains deferasirox present in an amount of from 45% to 60% by weight based on the total weight of the tablet, and wherein the tablet contains 90 mg, 180 mg or 360 mg of deferasirox, wherein deferasirox is present in free acid form,wherein the tablet further comprises,

(i) at least one filler in a total amount of 10% to 40% by weight based on total weight of the tablet, wherein the filler is microcrystalline cellulose;
(ii) at least one disintegrant in a total amount of 1% to 10% by weight based on the total weight of the tablet, wherein the disintegrant is cross-linked polyvinylpyrrolidone (crospovidone);
(iii) at least one binder in a total amount of 1% to 5% by weight based on the total weight of the tablet, wherein the binder is polyvinylpyrrolidone (PVP);
(iv) at least one surfactant in a total amount of up to 2% by weight based on the total weight of the tablet, wherein the surfactant is poloxamer;
(v) at least one glidant in a total amount of 0.1% to 1% by weight based on the total weight of the tablet, wherein the glidant is colloidal silicon dioxide;
(vi) at least one lubricant in a total amount of less than 0.1% to 2% by weight based on the total weight of the tablet, wherein the lubricant is magnesium stearate; and
(vii) a coating

and wherein the tablet does not contain sodium lauryl sulfate and does not contain lactose."

Claims 2 to 4 of the main request correspond to granted claims 2 to 4 wherein the feature "or a pharmaceutically acceptable salt thereof" was deleted.

VIII. The following items of evidence were filed by the parties during the appeal proceedings:

(a) Documents filed by the appellant - patent proprietor with its reply to the statements setting out the grounds of appeal (D41) and with the letters of 21 April 2022 (D42 and D43, filed as D41) and 21 December 2022 (D45):

D41: SmPC for Exjade dispersible tablets, 2006
D42: F. Liu, E. McConnell, S. Pygall, Update on Polymers for Oral Drug Delivery, 2011, page 20
D43: Statement of agreed common general knowledge between the parties from the UK proceedings (Claim No. HP-2021-000010)
D45: Opinion of the technical judge in Swiss proceedings O2021_004, O2021_005, 6 October 2022 (original German version and certified English translation)

(b) Document filed by appellant - opponent 2 with the letter of 14 December 2022:

D44: First instance judgment in UK proceedings Teva v Novartis [2022] EWHC 2847 (Pat), 10 November 2022

IX. Oral proceedings were held before the Board on 25 January 2023.

X. Each of appellant - opponent 1 and appellant - opponent 2 requested that the decision under appeal be set aside and that the patent be revoked.

Appellant - opponent 2 further requested document D45 not be admitted into the appeal proceedings, should document D44 not be admitted.

XI. The appellant - patent proprietor requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request filed with the reply to the statements setting out the grounds of appeal on 22 February 2022 as auxiliary request 48, or that the patent be maintained on the basis of one of the auxiliary requests 1 to 71 submitted with the reply to the statements setting out the grounds of appeal wherein auxiliary request 48 was the request originally filed as the main request.

The appellant - patent proprietor further requested the inventive step attack based on document D1 and the clarity attack against auxiliary request 48 (filed as main request with the reply to the statements setting out the grounds of appeal) raised by the appellant - opponent 2 not be admitted into the appeal proceedings.

The appellant - patent proprietor also requested document D44 not be admitted into the appeal proceedings. Should it be admitted, the appellant - patent proprietor requested document D45 to be admitted into the appeal proceedings.

XII. The arguments of the appellant - patent proprietor, as far as relevant for the present decision, can be summarised as follows:

(a) D44 was late-filed and not to be admitted into the appeal proceedings. The judgement was complex and not suitable to resolve the issues raised in the present proceedings. Should D44 be admitted into the appeal proceedings, then D45 was also to be admitted to provide a balanced picture of the opinions of national courts on the patent.

(b) The main request did not infringe Article 123(3) EPC.

(c) The main request met the requirements of Article 123(2) EPC. The subject-matter of independent claim 1 was directly and unambiguously derivable from the original claims and description.

(d) The inventive step attack starting from D1 was not to be admitted into the appeal proceedings. It did not form part of the appeal case of the appellants - opponents according to Article 12(2) RPBA 2020 and should not be admitted into the appeal proceedings under Article 12(4) RPBA 2020.

(e) D3 should be considered as the closest prior art. However starting from D7 as closest prior art, the claimed tablet differed from the one of example 26 of D7 in:
(i) the presence of a film coating,
(ii) the specific absolute amount of deferasirox,
(iii) the absence of SLS and lactose,
(iv) the presence of poloxamer, and
(v) that it was swallowable.
The claimed tablet had an improved bioavailability, at least compared to Exjade™, as well as an improved palatability and convenience of

administration. The objective technical problem resided consequently in the provision of a more palatable and convenient deferasirox tablet that had improved bioavailability (or at least good bioavailability). None of the prior art documents indicated that a swallowable tablet of deferasirox could be prepared while achieving said bioavailability, let alone when omitting lactose and SLS and adding poloxamer. Hence, the main request complied with the requirements of Article 56 EPC.

XIII. The arguments of the appellants - opponents, as far as relevant for the present decision, can be summarised as follows:

(a) Appellant - opponent 2 considered that D44 was to be admitted into the appeal proceedings. D44 could not have been filed earlier and was relevant since it kept the Board up to date concerning national proceedings regarding the patent. Should D44 be admitted into the proceedings, appellant - opponent 2 was not opposed to the admittance of D45.

(b) Appellant - opponent 1 considered that the scope of protection extended beyond the one defined by the granted patent, because the tablets according to present claim 1 could contain a pharmaceutically acceptable salt of deferasirox in an amount higher than the one defined in granted claim 1.

(c) Both appellants - opponents considered that the subject-matter of claim 1 of the main request extended beyond the original disclosures of the present application and the earlier application. In particular, the combination of the specific

excipients with the amounts for each type of excipient claimed in present claim 1 would not be originally disclosed. Moreover, appellant - opponent 1 argued that the introduction of the feature "deferasirox present in free acid form" amounted to an unallowable intermediate generalisation of the original disclosures.

(d) The inventive step attack starting from D1 was to be admitted into the appeal proceedings. This attack had not been abandoned during opposition proceedings even if the discussion during oral proceedings concentrated on D7 as closest prior art. It was reasonable to present a full case in the appeal proceedings.

(e) D7 represented the closest prior art. Example 26 but also examples 16 and 39 of D7 could be considered as the closest examples. The claimed tablet differed from the one of example 26 of D7 in:

(i) the presence of a film coating,
(ii) the specific absolute amount of deferasirox,
(iii) the absence of SLS and lactose, and
(iv) the presence of poloxamer.

The feature "swallowable" was not defined in the patent nor did it have a commonly recognised meaning. The tablet of claim 1 of the main request had thus merely to be suitable for swallowing. Since the size and excipients of the tablets of D7 rendered them suitable for swallowing, this feature was not a distinguishing feature.

No effect compared to the closest prior and linked to any of the distinguishing features had been

appropriately substantiated. During oral proceedings, both appellants - opponents referred to the objective technical problem as the provision of a deferasirox formulation having good bioavailability.

Swallowable tablets were the most common oral dosage forms. In view of D7 and D37, the skilled person would have expected swallowable tablets of deferasirox to have a good bioavailability. Furthermore, the skilled person would have replaced lactose and SLS, known to cause intolerance issues and gastrointestinal (GI) irritations, by alternative excipients listed in D7, while still expecting a good bioavailability. Providing a film coating was a routine measure when preparing tablets, in particular to improve palatability. The absolute amounts of deferasirox claimed corresponded to convenient doses which were obvious for the skilled person. It followed that the main request did not comply with the requirements of Article 56 EPC.

Reasons for the Decision

1. Admittance of D44 and D45

1.1 D44 and D45 correspond to an appealable decision of the UK national court (D44) and a technical opinion of the Swiss national court (D45) in national proceedings concerning the present patent.

It is established Case Law that, in the interest of the harmonisation of national and international rules of law, the boards of appeal will take into consideration decisions and opinions given by national courts in

interpreting the law (see G 5/83 Second medical indication/EISAI (OJ EPO 1985, 64), Reasons No. 6). Nevertheless, as stated in T 154/04, in the proceedings before the European Patent Office, such considerations do not exonerate a board of appeal from its duty as an independent judicial body to interpret and apply the European Patent Convention and to decide in last instance in patent granting matters.

In the present case, the Board considers the filing of D44 and D45 as being of informative nature regarding respectively the outcome (D44) and progress (D45) of national proceedings concerning the present patent. Furthermore, given their dates of issuance these documents could not have been submitted earlier, which constitutes exceptional circumstances in the sense of Article 13(2) RPBA 2020. These documents are thus admitted into the appeal proceedings. The Board underlines however that it is not bound by any of the conclusions reached in these documents.

Main request

2. Amendments

2.1 Article 123(3) EPC

2.1.1 Claim 1 of the main request corresponds to granted claim 1 wherein:
(a) the tablets were specified as "swallowable",
(b) the reference to a pharmaceutically acceptable salt of deferasirox as alternative to deferasirox was deleted and deferasirox was specified as "present in free acid form",
(c) the presence of a surfactant is mandatory (deletion of "optionally"), and

(d) the tablets were limited to tablets not containing SLS and lactose.

2.1.2 The modifications (a), (c) and (d) were not objected to under Article 123(3) EPC. The Board considers that these modifications do not extend the scope of protection.

2.1.3 Regarding modification (b), appellant - opponent 1 argued that, due to the open formulation of claim 1 of the main request ("contains" and "comprises"), a pharmaceutically acceptable salt of deferasirox could be further contained in any amount. However granted claim 1 limited the amount of such a salt to 90 mg, 180 mg or 360 mg. It followed that tablets according to present claim 1 could contain a pharmaceutically acceptable salt of deferasirox in an amount higher than the one defined in granted claim 1. The scope of protection had thus been extended.

2.1.4 This argument is not convincing. The Board considers that the specification of deferasirox being in free acid form, despite the otherwise open formulation of the claims, implicitly includes the proviso that deferasirox in any other form is not contained in the formulation. As a result a tablet according to claim 1 cannot encompass any deferasirox salt at all. The scope of protection conferred by present claim 1 does thus not extent beyond the one of the granted patent. The same applies by way of dependency to claims 2-4 of the main request.

2.2 Article 76(1) and 123(2) EPC

2.2.1 The patent was filed as a divisional application of the earlier European patent application No. 14 710 654.6

(earlier application). The following considerations refer to the disclosure of the presently claimed subject-matter in the original earlier application (Article 76(1) EPC). It is undisputed that the original descriptions of the earlier application and present divisional application are identical. These considerations thus apply *mutatis mutandis* for the disclosure of the presently claimed subject-matter in the original application (Article 123(2) EPC).

2.2.2 Claim 1 corresponds to the embodiment disclosed in the paragraph bridging pages 3 and 4 of the original earlier application wherein:
(a) the tablet was specified as "swallowable",
(b) the tablet was specified as "film" coated,
(c) the relative amount of active ingredient (drug load) was specified,
(d) the absolute amount of active ingredient (dose) was specified
(e) each class of excipient was limited to a specific excipient,
(f) deferasirox was specified as being present in free acid form, and
(g) the feature "the tablet does not contain sodium lauryl sulfate and does not contain lactose" was introduced.

2.2.3 Regarding the modification (a), the Board observes that the earlier application as originally filed contains several literal references to "swallowable" tablets, see for example page 6, fourth paragraph. It appears furthermore directly and unambiguously derivable that this feature applies to any of the tablets disclosed in the original earlier application, including those disclosed in the paragraph bridging original pages 3 to 4. The considerations regarding the interpretation of

the term "swallowable" made by the appellants - opponents do not appear relevant for the assessment of compliance with the requirements of Article 76(1) EPC.

2.2.4 Film coated tablets (feature (b)) containing the presently claimed dose of deferasirox are disclosed on page 6, last paragraph of the original earlier application. The relative amount of active ingredient (feature (c)) is disclosed in the original earlier application, for example on page 3, third paragraph and page 9, third paragraph in the context of coated tablets. It appears directly and unambiguously derivable that these features apply to any of the tablets disclosed.

2.2.5 The absolute amounts of deferasirox (modification (d)) are disclosed on page 6, last paragraph of the original earlier application. These amounts are defined in the same way as in present claim 1, *i.e.* with respect to deferasirox as such.

2.2.6 Regarding modification (e), the appellants - opponents were of the opinion that the combination of the specific excipients with the amounts for each type of excipient claimed in present claim 1 would not be originally disclosed.

The Board observes that the relative amounts of excipients are indeed defined in the paragraph bridging pages 3 and 4 of the original earlier application with respect to classes of excipients, namely filler, disintegrant, binder, surfactant, glidant and lubricant.

As argued by the appellant - patent proprietor, crospovidone, povidone (PVP), colloidal silicon dioxide

and magnesium stearate are disclosed in the original earlier application as the preferred disintegrant, binder, glidant and lubricant (see page 8, paragraphs 1, 2, 4 and 5). Furthermore microcrystalline cellulose (MCC) is the sole filler disclosed in the original earlier application (see page 7, last paragraph).

In the contested decision, the opposition division considered that the restriction of the surfactant to "poloxamer" in combination with these other restrictions extended the subject-matter claimed since "poloxamer" was not disclosed at the same level of preference as the other specific excipients. The preferred surfactant would be the more specific poloxamer 188.

As argued by the appellant - patent proprietor, the choice of specific excipients in present claim 1 appears to follow a consistent approach in which the preferred excipient in each class was selected without however specifying particular trademark grades. For example, MCC and PVP were chosen as filler and binder instead of the more specific Avicel® and PVP K30™ products. The same level of preference appears to have been applied for the surfactant, *i.e.* poloxamer instead of the specific Pluronic™ F68 grade (*i.e.* poloxamer 188), see page 8, paragraph 3 of the original earlier application. The Board considers that it would not be appropriate to make a distinction between Pluronic™ F68 grade and the other tradenames only because Pluronic™ F68 grade can be referred to by a non-proprietary name "poloxamer 188".

Hence, each of the presently claimed excipients was individualised in the description of the original earlier application. It is directly and unambiguously

derivable that the specific excipients individualised in the paragraphs on page 8 of the original earlier application apply to any of the disclosed tablets, including those described in the paragraph bridging pages 3 and 4 of the original earlier application. Therefore, contrary to the opinion of appellant - opponent 1, there is a 1 to 1 correspondence between the specific preferred excipients disclosed on original page 8 of the earlier application and the classes of excipients disclosed in the paragraph bridging original pages 3 and 4 of the earlier application.

The fact that excipients may have more than one function, and that MCC is actually listed as suitable binder and disintegrant in the earlier application (see original page 8), would not prevent the skilled person from recognising that each specific excipient of one embodiment corresponds to one class of excipients of the other embodiment. The fact that, in the embodiment on pages 3 to 4 of the original earlier application, the wording "at least one" is used would not lead the skilled person to consider some specific excipients of page 8 of the original earlier application to be used for various functions, in particular not a function for which another excipient is disclosed as preferred.

2.2.7 Appellant - opponent 1 argued that there was no *verbatim* disclosure in the original earlier application for feature (f) *per se*. The sole mention of deferasirox present in free acid form was original claim 12 of the earlier application. However this feature was disclosed only in combination with a specific amount of deferasirox, namely 50 mg to 600 mg. The introduction of feature (g) in present claim 1 constituted therefore an unallowable intermediate generalisation.

The Board considers that, as explained in the first instance decision (see item 27.9), it is clear in view of the formula of deferasirox (see paragraph bridging pages 2 and 3 of the original earlier application) that "deferasirox" in the context of the earlier application as originally filed, when not referring to a pharmaceutically acceptable salt, refers to the free acid. Moreover, this is actually confirmed by original claim 12 of the earlier application (disclosed as embodiment 12 on page 29 of the original application). Since the presently claimed absolute amounts are disclosed on page 6, last paragraph of the original earlier application with respect to "deferasirox" (and not any salt thereof) and fall within the broad range of amounts defined in said claim 12, the argument regarding an unallowable intermediate generalisation is not convincing.

2.2.8 The appellants - opponents did not raise any objection against the introduction of feature (g). The appellant - patent proprietor explained that this feature was disclosed in the original earlier application in the first paragraph under the heading "Detailed Description of the Invention" on page 6 as well as in the third paragraph on page 7 and in last bullet point on page 21.

2.3 Accordingly, the Board comes to the conclusion that the main request complies with the requirements of Article 76(1), 123(2) and 123(3) EPC.

3. Sufficiency of disclosure and clarity

In the appeal proceedings, the appellants - opponents did not raise any objection of lack of sufficiency of disclosure or clarity applying to the main request. The

Board considers that the requirements of Articles 83 and 84 are fulfilled.

4. Inventive step

4.1 Admittance of the attack based on D1

4.1.1 The appellant - patent proprietor requested the inventive step attack based on D1 not be admitted into the appeal proceedings.

4.1.2 This attack was raised by appellant - opponent 2 in its statement setting out the grounds of appeal. It is undisputed that it had initially been raised in writing during the opposition proceedings. However, according to the minutes of the oral proceedings, the choice between D3, D7 and D27 as closest prior art was discussed during oral proceedings in opposition but no other document was considered by any opponent. None of the appellants - opponents requested a correction of the minutes. In line with T 2730/16 (see point 4.2 of the Reasons), the Board considers that the attack starting from D1 was not actively maintained.

4.1.3 The absence of mention of the attack based on D1 in the impugned decision further confirms that this attack was implicitly abandoned.

4.1.4 It follows that this attack does not form part of the appeal proceedings according to Article 12(2) RPBA 2020. Its admittance into the appeal proceedings is thus at the discretion of the Board according to Article 12(4) RPBA 2020.

4.1.5 The implicit abandonment of this attack by appellant - opponent 2 prevented the decision from being based

thereupon. A re-introduction of this attack would be against the purpose of the appeal proceedings to constitute a judicial review of the appealed decision and against procedural economy.

4.1.6 Accordingly this attack is not admitted into the appeal proceedings (Article 12(4) RPBA 2020).

4.2 Closest prior art

4.2.1 The patent relates to deferasirox tablets and aims at re-formulating the current dispersible tablets into swallowable tablets so as to increase the drug load while maintaining equivalent PK profile, and consequently increase the therapeutic outcome as compared to commercially marketed Exjade™ dispersible tablets (see paragraph [0006]). According to the patent, the disclosed tablets have higher bioavailability than commercially marketed Exjade™ dispersible tablets (see paragraph [0009]).

4.2.2 During oral proceedings all parties developed their arguments starting from D7 as closest prior art. However, during the written proceedings, the appellant - patent proprietor argued that D3 represented a better starting point for the assessment of inventive step and appellant - opponent 2 considered that D27 would also represent a valid starting point.

4.2.3 According to established case law (see Case Law of the Boards of Appeal of the EPO, 10th Edition, 2022, I.D. 3.1., first paragraph), the closest prior art for assessing inventive step is normally a prior art document disclosing subject-matter conceived for the same purpose or aiming at the same objective as the claimed invention and having the most relevant

technical features in common, *i.e.* requiring the minimum of structural modifications. A further criterion for the selection of the most promising starting point is the similarity of the technical problem.

4.2.4 D7 is the only cited document which explicitly mentions the aim of improving bioavailability (see paragraph [0016]). While the examples of D7 concentrate on dispersible tablets, the preparation of other oral dosage forms is also generally considered (see *e.g.* paragraphs [0023], [0059], [0061]). Furthermore D7 discloses compositions having similar excipients as the present ones and relative amounts of deferasirox corresponding to the present claimed range.

4.2.5 D3 mentions tablets with a high drug load per se, but it is not concerned with PK profile of the dosage forms. Furthermore the tablet of example 2 relied upon by the appellant - patent proprietor has a relative amount of deferasirox which is below the one defined in present claim 1 and D3 is clearly restricted to dispersible tablets. Thus D3 does not address the same purpose regarding bioavailability as the patent and the disclosed tablets are structurally more remote than the tablets of D7.

4.2.6 The appellant - patent proprietor argued that D3 would be a better starting point because the tablet of example 2 corresponds to commercial Exjade™ tablets, for which clinical data are available. However this is not indicated in D3. Knowledge of the composition of commercial Exjade™ tablets is thus required to become aware of this fact. Moreover, D3 per se does not provide any PK or clinical data. Hence, D3 is less

suitable than D7 as starting point for the assessment of inventive step.

4.2.7 D27 is the basic patent for deferasirox, disclosing compounds *per se* for use in treatment of metal overload. D27 does not concentrate on the formulation of the active compounds, let alone pharmacokinetic properties. Example A is merely a prophetic example and differs from the present tablets in the nature of almost all the excipients. D27 does therefore not constitute an alternative to D7 as closest prior art.

4.2.8 Accordingly, the Board considers D7 as the closest prior art document. During oral proceedings, all parties considered example 26 as starting point within D7. Concerning the attacks based on examples 16 and 39 presented by appellant - opponent 1 in the written proceedings, the Board observes that, independently of the issue of their admittance, all three examples 26, 16 and 39 of D7 differ from the subject-matter of present claim 1 by the same distinguishing features. It follows that the reasoning developed below starting from example 26 applies *mutatis mutandis* from each of the two other starting points.

4.3 Distinguishing features

4.3.1 The following distinguishing features between the tablets according to claim 1 and the one of example 26 of D7 were undisputed:

(i) presence of a film coating,

(ii) specific absolute amount of deferasirox,

(iii) absence of SLS and lactose, and

(iv) presence of poloxamer.

4.3.2 However, the parties disagreed as to whether the feature "swallowable" constituted a distinguishing feature *versus* the dispersible tablet of example 26 of D7 or not.

4.3.3 The first issue is the interpretation of the feature "swallowable" in present claim 1. The Board considers "swallowable" as a tablet suitable to be orally ingested as it is *i.e.* without prior modification such as crushing, chewing or dispersing in water.

In this context, the Board disagrees with appellant - opponent 1 that this would amount to considering the intended use as a limiting feature of the claims. The Board agrees with appellant - opponent 1 that claim 1 is directed to a product *per se* merely suitable for being swallowed. However this imparts a number of variable structural features to the product (size, palatability, thickness, hardness, ...) and is as such limiting. As a consequence, a tablet which needs to be crushed (for example because too big) or dispersed before being orally ingested would not be according to the claims. Conversely, this does not mean that a tablet according to claim 1 cannot be crushed, dispersed, solubilised and then administered in a different manner but it does not have to, since it is suitable to be swallowed as such.

4.3.4 Turning now to the tablet of example 26 of D7, the question to be answered is whether it would be suitable for swallowing without prior modification. According to D7, the ingestion of a "dispersible" tablet requires prior dispersion (see paragraph [0029]). The Board considers therefore that the skilled person would not regard the "dispersible" tablet of example 26 as suitable for swallowing without prior dispersion.

In this context, appellant - opponent 1 argued that the size and the individual nature of excipients of the tablet of example 26 would allow the tablet to be swallowed. In particular, this tablet would be smaller than the Exjade™ tablet (see D7, paragraph [0098] and D22, page 22 final paragraph). This argument is however not convincing because not only the size of a tablet and the individual nature of the excipients are decisive for the suitability for swallowing. For example the overall palatability, the hardness or the shape of the tablet are expected to also have an impact.

The appellants - opponents did not provide any evidence that tablets of D7 may indeed be swallowed without prior dispersion.

Most of the arguments of the appellants - opponents relate to dispersible Exjade™ tablets, in particular based on D12 and D37. However, the dispersible Exjade™ tablets are not identical with the tablets of D7. Even if they contain the same excipients, the relative amounts thereof differ from one composition to the other, so that no conclusion for the tablets of D7 can be drawn based on observations made with dispersible Exjade™ tablets. Moreover, the Board observes that the actual mode of administration of the Exjade™ tablets in D12 is not specified (the mere absence of a reference to a solution does not mean that there was no prior dispersion). Regarding D37, the Board observes that the undispersed tablets were cut into smaller pieces and swallowed with the same amount of water as used to prepare the dispersions (see page 104, right-hand column, bottom of the first paragraph). This does not

correspond to the administration of a standard swallowable tablet.

4.3.5 Finally, contrary to the opinion of appellant - opponent 1, the burden of proof in the present case rests with the appellants - opponents (see Case Law of the Boards of Appeal, 10th Edition 2022, I.C.3.5.1)

4.3.6 The Board considers therefore that the claimed tablets further differ from the one of example 26 of D7 in that they are swallowable without prior dispersion.

4.4 Technical effects and objective technical problem

4.4.1 According to the appellant - patent proprietor, the combination of the distinguishing features provided (i) improved bioavailability and (ii) improved palatability and convenience.

Bioavailability (effect (i))

4.4.2 The appellant - patent proprietor argued that the patent and D13 would substantiate that the claimed tablet has a higher bioavailability than the commercial dispersible tablet Exjade™ (patent, see Example 5, Table 3 and Example 6; D13, see Study F2102 in particular paragraph spanning pages 19 and 20, Table 6 on page 23, top of page 21). Furthermore the improved dissolution of the tablet of example 26 of D7 compared to the commercial Exjade™ tablet (see D7 table on page 20) would be far lower than the increase of bioavailability of the present tablets compared to the commercial Exjade™ tablet. Since there was a correlation between bioavailability and dissolution rate, an improved bioavailability was to be expected

for the present tablet compared to the one of example 26 of D7.

4.4.3 The Board first observes that no direct comparison of a tablet according to claim 1 with the dispersible tablet of example 26 of D7 has been performed.

4.4.4 Furthermore, the Board considers that no conclusion can be drawn from the indirect comparison with dispersible Exjade™ tablets.

A different characteristic was indeed measured in each case, *i.e.* dissolution of the dispersible Exjade™ tablets and the tablet of D7 *versus* bioavailability of the dispersible Exjade™ tablets and the tablet according to the claimed invention. While some qualitative correlation between both characteristics might indeed be generally expected, this cannot be considered sufficient to render credible an improvement over the tablet of D7 in the present case. Both the dissolution rate of example 26 of D7 and the bioavailability of the tablet of the invention are higher than those of the dispersible Exjade™ tablet. The argument of the appellant - patent proprietor relies on the fact that the improvement of the dissolution rate for the tablet of D7 is lower than the improvement in term of bioavailability of the claimed tablet. In absence of a quantitative and not merely qualitative correlation, it cannot be concluded that the claimed tablet necessarily has an increased bioavailability compared to the tablet of example 26 of D7.

Furthermore, the Board notes that the actual effect for the claimed tablet seems to go against this expected correlation (lower dissolution rate and still increased

bioavailability, see Figures 2, 7A and 7B of the patent).

4.4.5 It remains however that good bioavailability, namely better than the commercial dispersible tablet Exjade™, has been substantiated for the claimed tablet (see Tables 2-3, paragraph [0051] and Figures 7A and 7B of the patent).

4.4.6 The appellants - opponents argued that the alleged effect could not be generalised to the entire scope of the claims as it could not be attributed to any specific distinguishing feature. It could thus be due to any other undefined feature of the tested tablets (such as particle size of deferasirox, use of wet granulation process, compression force).

This argument is not convincing.

Since the good bioavailability is not considered as an improvement over the closest prior art tablet, there is no requirement that it must have been shown to have its origin in a specific distinguishing feature over said closest prior art.

Furthermore, there is no indication in the patent that the further features mentioned by the appellants - opponents would be unusual in the tested tablets. The Board considers credible the fact that the good bioavailability obtained in the examples of the patent (see Tables 2-3, paragraph [0051] and Figures 7A and 7B of the patent) is achieved thanks to the excipients used and their formulation into a swallowable tablet. These features, in particular all the excipients of the examples, form part of the claims of the main request. An extrapolation of the good bioavailability

demonstrated in the examples of the patent to other tablets according to claim 1 of the main request and with otherwise standard features appears therefore reasonable. Moreover, the appellants - opponents have not provided any evidence in support of the fact that tablets according to present claim 1 would not have good bioavailability, *i.e.* a better bioavailability than the commercial dispersible tablet Exjade™.

4.4.7 In this context, appellant - opponent 2 argued for the first time during the oral proceedings that in particular no generalisation of the effect obtained for a tablet containing poloxamer 188 could be done for a tablet as presently claimed containing any type of poloxamer. Appellant - opponent 2 referred to D29, page 507 section 7 and table III which would substantiate that the properties of poloxamer vary over a wide range.

The appellant - patent proprietor requested this argument not be admitted into the appeal proceedings since there would be no exceptional reasons justifying its filing at such a late stage. Appellant - opponent 2 considered that the issue of generalisation of the effect over the entire scope had already been raised in its statement setting out the grounds of appeal in paragraph (91). Furthermore this argument was raised in the context of the conclusion reached by the Board on the previous day in the related case concerning the earlier application of the present patent (T 526/21) with respect to the lack of expectation of success. The same standard should indeed be applied to the expectation regarding the achievement of the effect over the whole claimed range.

Paragraph (91) of the statement setting out the grounds of appeal mentioned by appellant - opponent 2 reads as follows: "It is therefore apparent that the technical effect of bioavailability is not achieved by any of the distinguishing features. Even if it were accepted for the example in the patent, the patentee has not shown that the problem is solved across the whole scope of the claims. Bioavailability should not, therefore, be included in the definition of the objective technical problem.". The Board observes that this paragraph contains merely a general statement regarding the lack of substantiation of the effect over the whole scope of the claims, but does not refer at all to the newly raised issue concerning poloxamer 188 nor to D29. The argument raised during the oral proceedings does therefore constitute an amendment to the case of appellant - opponent 2.

Hence, its admittance at this late stage of the proceedings is to be decided based on Article 13(2) RPBA 2020. The Board does not recognise any exceptional circumstances which would justify the admittance of this argument at this late stage of the proceedings for the reasons detailed below. The present main request was indeed already filed with the statement setting out the grounds of appeal as auxiliary request 48 and D29 formed already part of the first instance proceedings. Also the initial main request filed with the statement of grounds of the appellant - patent proprietor, which was extensively discussed by the parties in the writing proceedings, already contained the feature "poloxamer". Finally, the conclusion reached by the Board in the related case T 526/21 was based on arguments of the parties provided in the written proceedings of T 526/21 and similar to arguments provided in the present written proceedings.

As a result, the new argument raised by appellant - opponent 2 concerning the generalisation of the technical effect in relation to the use of poloxamer as surfactant is not admitted into the appeal proceedings (Article 13(2) RPBA 2020).

Palatability (effect (ii))

4.4.8 Improved palatability compared to dispersible tablets may be considered credible due to film coating in combination with the suitability to be swallowed directly. The argument of appellant - opponent 1 that a bad tasting film coating would be encompassed by the claims is indeed not convincing since claim 1 foresees that the tablet be swallowed as such. Moreover, improving palatability is a known purpose of film coatings (see D39, page 131 1st entry in table; D33, page 858, bottom of right hand-column; D34 paragraph 3.27). In this context, appellant - opponent 1 stated that there was no indication in D7 that the dispersible tablets would not be palatable. However, the Board considers that it is generally admitted that dispersions are less palatable than film coated tablets. Appellant - opponent 1 has not provided any evidence supporting that it would not be the case for the present tablets compared to dispersible tablets of D7.

Objective technical problem

4.4.9 It follows that, starting from D7, the objective technical problem resides in the provision of a deferasirox formulation having improved palatability and good bioavailability.

4.5 Obviousness

4.5.1 The improved palatability having been considered credible based on common general knowledge, it cannot confer inventiveness to the present tablets. The provision of a film coating to this aim is therefore obvious.

4.5.2 The specific absolute amounts of deferasirox of present claim 1 appear to constitute obvious modifications of known specific doses within usually used ranges. This feature cannot therefore provide inventiveness to the claimed tablet. This was not disputed.

4.5.3 As argued by the appellants - opponents, the skilled person would have been aware of the potential drawbacks in terms of gastrointestinal irritation and tolerance linked to the presence of SLS and lactose in the composition of D7 (see *e.g.* D28 and D29). D7 generally discloses microcrystalline cellulose (MCC) as one of the alternative excipients to lactose (see paragraphs [0054] and [0080]) as well as poloxamer as a suitable surfactant (see paragraph [0066]). The individual replacement of SLS and lactose in the formulation of example 26 of D7 by for example poloxamer and MCC might have appeared obvious to the skilled person willing to avoid the above mentioned drawbacks.

Furthermore, the idea of providing a swallowable tablet to improve the ease of administration may appear obvious *per se*.

4.5.4 However, in the present case, the key point is whether good bioavailability would have been expected for a swallowable tablet of deferasirox with the claimed excipients. The Board observes that dispersible tablets

are generally expected to have a better bioavailability than swallowable tablets, as confirmed by D18 (see page 296, left column, first full paragraph). The skilled person would therefore have had no reasonable expectation of success of achieving good bioavailability when formulating deferasirox as a swallowable film coated tablet, let alone with the present excipients.

4.5.5 The appellants - opponents argued that the bioavailability ranking of dosage forms provided in D18 was however not an absolute rule and that, in the specific case of deferasirox, experimental data were actually available (see D37, treatment A versus treatments B to D) indicating that the dispersion would have no influence on the bioavailability. According to these data, whether the Exjade™ tablet was dispersed or not before administration, the bioavailability remained unaffected. As a consequence, the skilled person would have learned from D37 that in the case of deferasirox, dispersion would have no influence on bioavailability. Furthermore a dispersible tablet would merely be one embodiment of D7, which also described oral dosage forms as alternatives to dispersible tablets (see paragraphs [0023], [0059] and [0061]). The aim of D7 being good bioavailability (see paragraphs [0013] to [0016]), it would be expected for any formulation disclosed in D7. During oral proceedings, appellant - opponent 1 underlined in this context that example 26 of D7 has an improved dissolution compared to Exjade™ which is at least qualitatively indicative of a good bioavailability. The appellants - opponents thus concluded that the skilled person would have expected that, by modifying the dispersible tablet of example 26 of D7 into a swallowable tablet, good bioavailability would be maintained.

4.5.6 This argument is however not convincing.

The purpose of D37 was to study the impact on bioavailability of an administration of commercial dispersible Exjade™ tablets which would not be according to registration study, *i.e.* dispersion in a different medium or uncomplete dispersion.

Treatment A of D37 indeed corresponds to the administration of an Exjade™ tablet cut into pieces and swallowed without prior dispersion. However, contrary to the argumentation developed by the appellants - opponents, the Board considers that no indication regarding the bioavailability of film coated swallowable tablets can be inferred from this study.

Film coated swallowable tablets contain *per* definition different excipients in different amounts than dispersible tablets. In particular a dispersible tablet is made such as to dissolve fast in an appropriate liquid. This is not the case of a film coated swallowable tablet. Even if, as argued by appellant - opponent 2 during oral proceedings, both type of tablets contain a disintegrant, the relative amount thereof is usually higher in a dispersible tablet (20% crospovidone in Exjade™, see D3 example 2, which was indicated by the parties as representing the composition of Exjade™) as in a film coated swallowable tablet (1-10%, see paragraph [0012] of the patent).

Moreover, in D37 treatment A the tablet was administered with the same volume of water as the one used to disperse the tablets prior to administration in treatments B and C. These conditions do not represent

standard administration of a swallowable tablet. In the case of D37 treatment A it is indeed to be expected that the large amount of water ingested with the tablet will participate to the dispersion of the tablet in the stomach.

Furthermore, as indicated by the appellant - patent proprietor during oral proceedings, the tablet "in the form of an oral dosage form" generally disclosed in D7 cannot be equated with a film coated swallowable tablet. While oral dosage form tablets encompass film coated swallowable tablets, they also encompass further types of tablets, such as chewable tablets or sublingual tablets. D7 does therefore not provide any hint that good bioavailability would be obtained when formulating deferasirox specifically in a film coated swallowable tablet.

As a result, the Board considers that neither the disclosure of D7 nor the results of D37 would have provided a reasonable expectation of success of good bioavailability when formulating deferasirox in film coated swallowable tablets.

4.5.7 As explained by the appellant - patent proprietor, the skilled person would furthermore be aware of the fact that SLS may contribute to the dissolution of the tablet of example 26 of D7. While its replacement by poloxamer so as to avoid GI irritation might have appeared obvious, there is no indication in the prior art documents that good bioavailability would indeed necessarily be obtained with such a replacement.

4.6 Accordingly, the main request fulfills the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The case is remitted to the opposition division with the order to maintain the patent on the basis of the claims of the main request filed as auxiliary request 48 with the reply to the statements setting out the grounds of appeal on 22 February 2022, and a description to be adapted.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated