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Datasheet for the decision of 24 January 2023

Case Number: T 0526/21 - 3.3.07

Application Number: 14710654.6

Publication Number: 2964202

IPC: A61K9/20, A61K9/28, A61K9/50, A61K31/4196, A61P39/04

Language of the proceedings: EN

Title of invention:
ORAL FORMULATIONS OF DEFERASIROX

Patent Proprietor:
Novartis AG

Opponents:
Teva Pharmaceutical Industries Ltd.
HGF Limited
INVOKAT Intellectual Property Services

Headword:
Oral Formulations of Deferasirox / NOVARTIS

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

Keyword:
Item of evidence filed after summons - admitted (yes)
Amendments - allowable (yes)
Inventive step - no reasonable expectation of success
Amendment to case - amendment admitted (no)

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

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Case Number: T 0526/21 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 24 January 2023

Appellant 1: (Opponent 1)	Teva Pharmaceutical Industries Ltd. 124 Dvora HaNevi'a St. 6944020 Tel Aviv (IL)
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Appellant 2: (Opponent 2)	HGF Limited 1 City Walk Leeds Yorkshire LS11 9DX (GB)
Representative:	HGF HGF Limited 1 City Walk Leeds LS11 9DX (GB)
Respondent: (Patent Proprietor)	Novartis AG Lichtstrasse 35 4056 Basel (CH)
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Party as of right: (Opponent 3)	INVOKAT Intellectual Property Services Kartaltepe Mh. Yildiztepe Sk. No: 6 Bakirköy 34145 Istanbul (TR)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 17 March 2021 concerning maintenance of the European Patent No. 2964202 in amended form.**

Composition of the Board:

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

Summary of Facts and Submissions

I. European patent 2 964 202 (hereinafter "the patent") was granted on the basis of 5 claims. The independent claim of the patent as granted read as follows:

"1. A film coated tablet for oral administration comprising deferasirox or a pharmaceutically acceptable salt thereof present in an amount from 45% to 60% by weight based on the total weight of the tablet, wherein the tablet is without sodium lauryl sulfate and lactose, and comprises
(i) microcrystalline cellulose;
(ii) crospovidone;
(iii) povidone;
(iv) poloxamer 188;
(v) colloidal silicon dioxide;
(vi) magnesium stearate."

II. Three oppositions were filed against the patent on the grounds that its subject-matter lacked inventive step and it extended beyond the content of the application as originally filed.

III. The opposition division took the interlocutory decision that, on the basis of the main request, the patent met the requirements of the EPC. The main request was filed with the letter of 28 February 2020. The independent claim 1 corresponded to granted claim 1 wherein the expression "film coated tablet for oral administration" had been replaced by "swallowable film coated tablet".

IV. The decision of the opposition division, posted on 17 March 2021, cited *inter alia* the following documents:

D1: WO 2010/143006 A1
D2: WO 2004/035026 A1
D4: Assessment report EMA/CHMP/107225/2016, published 28 January 2016
D6: Exjade: EPAR - Product Information Annex I published first published by European Medicines Agency on 20 August 2009
D9: WO 2009/067557 A1
D18: Eadala *et al.*, Alimentary Pharmacology and Therapeutics, Vol. 29, 2009, 677-687
D19: Rowe, Raymond C *et al.*, "Handbook of Pharmaceutical Excipients", 6th Edition, 2009, 506-509 and 651-653
D22: Allen, Jr. Loyd V. *et al.*, "Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems", 9th Edition, 2011, 128-132
D24: WO 2007/045445 A1
D28: Aulton, "Aulton's Pharmaceutics: The Design and Manufacture of Medicines", Third Edition, 2007, 293, 296-297, 451 and 455
D34: EP 0 914 118 B1
D38: "Remington: The Science and Practice of Pharmacy", 20th Edition, 2000, chapter 45
D39: Declaration from Peter Rue dated 11 December 2020 (and CV)
D42: R. Sechaud *et al.*, International Journal of Clinical Pharmacology and Therapeutics 2008, 46(2), 102-108

V. The opposition division decided *inter alia* that the main request complied with the requirements of Articles 123(2) and 123(3) EPC. Furthermore, starting from the closest prior art D9, the subject-matter of the main request involved an inventive step.

VI. Opponent 1 (appellant 1) and opponent 2 (appellant 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 patent proprietor (respondent) defended its case on the basis of the main request maintained during opposition proceedings (main request filed on 28 February 2020), and on the basis of auxiliary requests 1 to 35 filed therewith.

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

(a) Documents filed by the respondent with its reply to the statements setting out the grounds of appeal (D46) and with the letters of 21 April 2022 (D47 and D48) and 21 December 2022 (D50):

D46: SmPC for Exjade dispersible tablets, 2006
D47: Statement of agreed common general knowledge between the parties from the UK proceedings (Claim No. HP-2021-000010)
D48: F. Liu, E. McConnell, S. Pygall, Update on Polymers for Oral Drug Delivery, 2011, page 20
D50: Opinion of the technical judge in Swiss proceedings O2021_004, O2021_005, 6 October 2022 (original German version and certified English translation)

(b) Documents filed by appellant 1 with the letter of 14 December 2022:

D49: 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 24 January 2023.

X. Opponent 3 did not make any submission in the appeal proceedings and did not attend the oral proceedings.

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

Appellant 1 further requested document D50 not be admitted into the appeal proceeding, should document D49 not be admitted.

XII. The respondent requested that the appeal be dismissed, *i.e.* that the patent be maintained as amended during first instance proceedings (main request), or that the patent be maintained on the basis of one of the auxiliary requests 1 to 35 submitted with the reply to the statements setting out the grounds of appeal.

The respondent further requested the inventive step attacks based on D24, D34 and examples 16 and 39 of D9 not be admitted into the appeal proceedings.

The respondent also requested document D49 not be admitted into the appeal proceedings. Should it be admitted, the respondent requested document D50 to be admitted into the appeal proceedings.

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

(a) Appellant 1 considered that D49 was to be admitted into the appeal proceedings. D49 could not have

been filed earlier and was relevant since it kept the Board up to date concerning national proceedings regarding the patent. Should D49 be admitted into the proceedings, appellant 1 was not opposed to the admittance of D50.

(b) Both appellants considered that the subject-matter of claim 1 of the main request extended beyond the original disclosure. In particular, the generalisation of the embodiment disclosed on original page 7 containing an Opadry coating to any film coating was not allowable. The Opadry coating constituted an essential feature of this embodiment which was inextricably linked to other features thereof such as poloxamer 188 and the absence of SLS and lactose. Moreover, according to appellant 2, dependent claim 2 infringed Article 123(2) EPC because the claimed combination of the specific excipients with the amounts for each type of excipient was not originally disclosed.

(c) The inventive step attacks starting from D24 and D34 were to be admitted into the appeal proceedings. These attacks had not been abandoned during opposition proceedings even if the discussion during oral proceedings concentrated on D9 as closest prior art. It was reasonable to present a full case in the appeal proceedings. Furthermore, appellant 2 considered that the present case would differ from the one underlying T 2730/16 because in the present case the appellants did contest the choice of the closest prior art in their written submissions in response to the preliminary opinion of the opposition division (see Rule 116 submission of appellant 1 of 11 December 2020, paragraphs 17 and 19 and letter

of appellant 2 of 11 December 2020 paragraphs 8 to 12).

(d) D9 represented the closest prior art. Example 26 but also examples 16 and 39 of D9 could be considered as the closest examples. The claimed tablet differed from the one of example 26 of D9 in:
(i) the presence of a film-coating,
(ii) the absence of SLS and lactose, and
(iii) the presence of poloxamer 188.
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 D9 rendered them suitable for swallowing, this feature was not a distinguishing feature.

No effect compared to the closest prior art and linked to any of the distinguishing features had been appropriately substantiated. During oral proceedings, both appellants formulated 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 D9 and D42, 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) irritation, by alternative excipients listed in D9, while still expecting a good bioavailability. Providing a film-

coating was a routine measure when preparing tablets, in particular to improve palatability. It followed that the main request did not comply with the requirements of Article 56 EPC.

XIV. The arguments of the respondent, as far as relevant for the present decision, can be summarised as follows:

(a) D49 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 D49 be admitted into the appeal proceedings, then D50 was also to be admitted to provide a balanced picture of the opinions of national courts on the patent.

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

(c) The inventive step attacks starting from D24 and D34 were not to be admitted into the appeal proceedings. They did not form part of the appellants' appeal case according to Article 12(2) RPBA 2020 and should not be admitted into the appeal proceedings under Article 12(4) RPBA 2020.

(d) D2 should be considered as the closest prior art. However starting from D9 as closest prior art, the claimed tablet differed from the one of example 26 of D9 in:
(iv) the presence of a film-coating,
(v) the absence of SLS and lactose,
(vi) the presence of poloxamer 188, and
(vii) 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 188. Hence, the main request complied with the requirements of Article 56 EPC.

Reasons for the Decision

1. Admittance of D49 and D50

1.1 D49 and D50 correspond to an appealable decision of the UK national court (D49) and a technical opinion of the Swiss national court (D50) in national proceedings concerning the present patent.

1.2 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 (OJ EPO 2008, 46; Reasons No. 3), 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.

1.3 In the present case, the Board considers the filing of D49 and D50 as being of informative nature regarding respectively the outcome (D49) and progress (D50) of national proceedings concerning the present patent. Furthermore, D49 and D50 were both issued after notification of the summons to oral proceedings, 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 Claim 1

2.1.1 Claim 1 corresponds to the embodiment disclosed on original page 7, third paragraph relating to film coated tablets wherein:
(a) the tablets were specified as "swallowable",
(b) the relative amount of active ingredient was specified, and
(c) the Opadry coating was omitted.

2.1.2 Regarding the modification (a), the Board observes that the application as originally filed contains several literal references to "swallowable" tablets, see for example page 6, fourth paragraph. It is furthermore directly and unambiguously derivable that this feature applies to any of the tablets disclosed in the original application, including those disclosed on original page

7, third paragraph. The considerations regarding the interpretation of the term "swallowable" made by the appellants are not relevant for the assessment of compliance with the requirements of Article 123(2) EPC.

2.1.3 The Board further notes that the relative amount of active ingredient (modification (b)) is individually disclosed in the original description, for example on page 3, third paragraph and page 9, third paragraph. It is directly and unambiguously derivable that this individually disclosed feature applies to any of the tablets disclosed.

2.1.4 The major point of dispute concerns the modification (c). The parties considered the omission of Opadry coating as an intermediate generalisation of the embodiment disclosed on original page 7, third paragraph. According to established case law of the Boards of appeal, an intermediate generalisation is justified only in the absence of any clearly recognisable functional or structural relationship among the features of the specific combination or if the extracted feature is not inextricably linked with those features (see Case Law of the Boards of Appeal of the EPO, 10th Edition, 2022, II.E.1.9.1 fourth paragraph).

The Board observes that the embodiment on original page 7, third paragraph starts by generally referring to "film coated tablets" including all the excipients listed in present claim 1. Only after is it mentioned that the coating material used in this embodiment was Opadry Blue, without specifying any function therefor beyond constituting the film coating. Contrary to the assertion of the appellants, it is thus not derivable from the literal wording of said paragraph, that

specifically the Opadry coating, and not any film coating, would be essential.

Furthermore, appellant 2 argued that the last sentence of the third paragraph of original page 7 indicates that Opadry Blue would be intrinsically linked to poloxamer 188 and to the absence of SLS and lactose. The Board disagrees. As mentioned by the respondent, this sentence appears to merely specify that these features constitute distinguishing features over commercial dispersible tablets without implying any interaction between the features. In this context, it is noteworthy that the removal of SLS and lactose to contribute to the reduction of GI irritation is generally disclosed on original page 6, fourth paragraph, without mentioning any link to the nature of the coating material.

Moreover, the specific excipients of the first sentence of the third paragraph on original page 7 correspond to the classes of excipients otherwise disclosed in combination in the original application without specifying any specific coating (see for example pages 3 to 4 and 9 to 10). This constitutes a pointer to the present combination of excipients without the specific Opadry coating.

Finally, the remaining parts of the original description refers in general terms to coated tablets, and Opadry Blue coated tablets as well as tablets coated with a different Opadry coating and/or an enteric coating are disclosed (see in particular examples 2 and 5, Variants B and C). The overall disclosure of the original application does not provide any essential character to Opadry blue coating, nor any particular interrelationship with any other excipient.

In this context, the argument of appellant 2 that Opadry coating would form a seal coat and thus protect poloxamer 188 from humidity is not convincing. As indicated by the respondent, the passage of the original application used by appellant 2 (see original claim 10) appears to refer to a different Opadry coating (Opadry 03K19229 i.e. Opadry Clear) than the one of original page 7, third paragraph (Opadry Blue). Furthermore the passage of D14 (see page 13, 3rd and 4th paragraph) also mentioned by appellant 2 in this context does not specifically refer to Opadry blue. Theses passages cannot thus be used to indicate any particular function of the specific coating material in original page 7, third paragraph over any film coating material. No such function was otherwise substantiated by the appellants.

Accordingly, the Board comes to the conclusion that the specific Opadry coating on original page 7, third paragraph is not related or inextricably linked to the other specific excipients disclosed in this embodiment beyond what any film coating material would be. It merely represents an example of a film coating. A composition comprising the specific excipients of original page 7, third paragraph and any film coating material is thus directly and unambiguously derivable from the original application.

2.2 Claim 2

2.2.1 Appellant 2 was of the opinion that dependent claim 2 infringed Article 123(2) EPC because the combination of the specific excipients with the amounts for each type of excipient would not be originally disclosed.

2.2.2 The Board observes that claim 2 depends on claim 1 and corresponds thus primarily to the embodiment on original page 7, third paragraph together with the features disclosed in original page 6, fourth paragraph ("swallowable") and original page 3, third paragraph or original page 9, third paragraph (relative amount of deferasirox).

2.2.3 Claim 2 further defines (i) the amounts of each of the excipients and (ii) that the coating comprises a functional or non-functional polymer. The amount ranges and the nature of the coating are disclosed in combination in one embodiment in the original application (see paragraph bridging pages 9 and 10). In this embodiment the ranges are indeed defined with respect to classes of excipients, namely filler, disintegrant, binder, surfactant, glidant and lubricant.

2.2.4 As argued by the respondent, crospovidone, povidone, poloxamer 188 (which is Pluronic™ F68 grade), colloidal silicon dioxide and magnesium stearate are disclosed in the original application as the preferred disintegrant, binder, surfactant, glidant and lubricant (see page 8, paragraphs 1 to 5). Furthermore microcrystalline cellulose (MCC) is the sole filler disclosed in the original application (see page 7 last paragraph). Hence, contrary to the opinion of appellant 2 there is a 1 to 1 correspondence between the specific excipients of the embodiment on original page 7, third paragraph and the classes of excipients disclosed in the paragraph bridging original pages 9 and 10. It is therefore directly and unambiguously derivable that the embodiment of original pages 9 to 10 defined in general terms applies to the specific embodiment of original page 7, third paragraph.

2.2.5 The fact that excipients may have more than one function, and that MCC is actually listed as suitable binder and disintegrant in the present 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 general embodiment on original pages 9 to 10, the wording "at least one" is used would not lead the skilled person to consider some specific excipients of original page 7, third paragraph to be used for various functions, in particular not a function for which another excipient is disclosed as preferred.

2.3 As a result, the subject-matter of claims 1 and 2 of the main request meets the requirements of Article 123(2) EPC. The remaining claims of the main request (claims 3 to 5) were not objected to by the appellants for lack of compliance with the requirements of Article 123(2) EPC. The appellants did furthermore not raise any objection under Article 123(3) EPC for the performed amendments. The subject-matter of claims 3 to 5 of the main request is disclosed in the original claims and the original description. Furthermore the scope of the claims was not broadened compared to the one of the granted claims. Hence, the main request complies with the requirements of Articles 123(2) and 123(3) EPC.

3. Inventive step

3.1 Admittance of attacks

3.1.1 The respondent requested the inventive step attacks raised by appellant 1 in its statement setting out the

grounds of appeal based on D24 and D34 not be admitted into the appeal proceedings.

3.1.2 The Board observes that the attacks based on D24 and D34 were raised in writing during the opposition proceedings in reply to the preliminary opinion of the opposition division (see submission of appellant 1 of 11 December 2020). However, the minutes of the opposition oral proceedings (see point 19.) indicate that "The three opponents agreed that D9 was the closest prior art. The proprietor argued that example 2 of D2 would be a better closest prior art [...]". According to the minutes, the choice between D2 and D9 as closest prior art was then discussed but no other document was considered by any opponent. None of the appellants requested a correction of the minutes. In line with T 2730/16, the Board considers that the attacks starting from D24 and D34 were not actively maintained.

3.1.3 The conclusion that the attacks based on D24 and D34 were implicitly abandoned or not raised in opposition proceedings is in line with the absence of mention thereof in the impugned decision.

3.1.4 It follows that these attacks do not form part of the appeal proceedings according to Article 12(2) RPBA 2020. Their admittance into the appeal proceedings is thus at the discretion of the Board according to Article 12(4) RPBA 2020.

3.1.5 The implicit abandonment of the attacks based on D24 and D34 by appellant 1 prevented the decision from being based thereupon. A re-introduction of these attacks would be against the purpose of the appeal

proceedings to constitute a judicial review of the appealed decision and against procedural economy.

3.1.6 Accordingly, these attacks are not admitted into the appeal proceedings (Article 12(4) RPBA 2020).

3.2 Closest prior art

3.2.1 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 [0008]).

3.2.2 During oral proceedings all parties developed their arguments starting from D9 as closest prior art. However, during the written proceedings, the respondent argued that D2 represented a better starting point for the assessment of inventive step.

3.2.3 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.

3.2.4 D9 is the only cited document which explicitly mentions the aim of improving bioavailability (see paragraph [0016]). While the examples of D9 concentrate on dispersible tablets, the preparation of other oral dosage forms is also generally considered (see *e.g.* paragraphs [0023], [0059], [0061]). Furthermore D9 discloses compositions having similar excipients as the present ones and relative amounts of deferasirox corresponding to the present claimed range.

3.2.5 On the other hand, D2 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 respondent has a relative amount of deferasirox which is below the one defined in present claim 1 and D2 is clearly restricted to dispersible tablets. Thus D2 does not address the same purpose regarding bioavailability as the patent and the disclosed tablets are structurally more remote than the tablets of D9.

3.2.6 The respondent argued that D2 would be a better starting point because the tablet of example 2 corresponded to commercial Exjade tablets, for which clinical data were available. However this is not indicated in D2. Knowledge of the composition of commercial Exjade™ tablets is thus required to become aware of this fact. Moreover, D2 *per se* does not provide any PK or clinical data. Hence, D2 is less suitable than D9 as starting point for the assessment of inventive step.

3.2.7 Accordingly, the Board considers D9 as the closest prior art document. During oral proceedings, all parties considered example 26 as starting point within D9. Concerning the attacks based on examples 16 and 39 presented by appellant 2 in the written proceedings, the Board observes that, independently of the issue of their admittance, all three examples 26, 16 and 39 of D9 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.

3.3 Distinguishing features

3.3.1 The following distinguishing features between the tablets according to claim 1 and the one of example 26 of D9 were undisputed:

(i) presence of a film-coating,

(ii) absence of SLS and lactose, and

(iii) presence of poloxamer 188.

3.3.2 However, the parties disagreed as to whether the feature "swallowable" constituted a distinguishing feature *versus* the dispersible tablet of example 26 of D9 or not.

3.3.3 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 2 that this would amount to considering the intended use as a limiting feature of the claims. The Board agrees

with appellant 2 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.

3.3.4 Turning now to the tablet of example 26 of D9, the question to be answered is whether it would be suitable for swallowing without prior modification. According to D9, 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 2 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 D9, paragraph [0098] and D6, 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 did not provide any evidence that tablets of D9 may indeed be swallowed without prior dispersion.

Most of the appellants' arguments relate to dispersible Exjade™ tablets, in particular based on D1 and D42. However, the dispersible Exjade™ tablets are not identical with the tablets of D9. 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 D9 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 D1 is not specified (the mere absence of a reference to a solution does not mean that there was no prior dispersion). Regarding D42, 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.

3.3.5 The Board considers therefore that the claimed tablets further differ from the one of example 26 of D9 in that they are swallowable without prior dispersion.

3.4 Technical effects and objective technical problem

3.4.1 According to the respondent, the combination of the distinguishing features provided (i) improved bioavailability and (ii) improved palatability and convenience.

Bioavailability (effect (i))

3.4.2 The respondent argued that the patent and D4 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; D4, 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 D9 compared to the commercial Exjade™ tablet (see D9 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 D9.

3.4.3 The Board first observes that no direct comparison of a tablet according to claim 1 with the dispersible tablet of example 26 of D9 has been performed.

3.4.4 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™ tablet and the tablet of D9 *versus* bioavailability of the dispersible Exjade™ tablet 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 D9 in the present case. Both the dissolution rate of example 26 of D9 and the bioavailability of the

tablet of the invention are higher than those of the dispersible Exjade™ tablet. The argument of the respondent relies on the fact that the improvement of the dissolution rate for the tablet of D9 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 D9.

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 and 4 of the patent).

3.4.5 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 [0050] and Figure 4 of the patent).

3.4.6 The appellants 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 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 [0050] and Figure 4 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 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™.

Palatability (effect (ii))

3.4.7 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 2 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 D22, page l31 1st entry in table; D38, page 858, bottom of right hand-column; D39 paragraph 3.27). In this context, appellant 2 stated that there was no

indication in D9 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 2 has not provided any evidence supporting that it would not be the case for the present tablets compared to dispersible tablets of D9.

Objective technical problem

3.4.8 It follows that, starting from D9, the objective technical problem resides in the provision of a deferasirox formulation having improved palatability and good bioavailability.

3.5 Obviousness

3.5.1 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.

3.5.2 As argued by the appellants, the skilled person would have been aware of the potential drawbacks in terms of GI irritation and tolerance linked to the presence of SLS and lactose in the composition of D9 (see *e.g.* D18 and D19). D9 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 D9 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 is obvious *per se*.

3.5.3 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 D28 (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.

3.5.4 The appellants argued that the bioavailability ranking of dosage forms provided in D28 was however not an absolute rule and that, in the specific case of deferasirox, experimental data were actually available (see D42, 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 D42 that in the case of deferasirox, dispersion would have no influence on bioavailability. Furthermore a dispersible tablet would merely be one embodiment of D9, which also described oral dosage forms as alternatives to dispersible tablets (see paragraphs [0023], [0059] and [0061]). The aim of D9 being good bioavailability (see paragraphs [0013] to [0016]), it would be expected for any formulation

disclosed in D9. The appellants thus concluded that the skilled person would have expected that, by modifying the dispersible tablet of example 26 of D9 into a swallowable tablet, good bioavailability would be maintained.

3.5.5 This argument is however not convincing.

The purpose of D42 was to study the impact on bioavailability of an administration of commercial dispersible Exjade™ tablets which would not be according to the registration study, *i.e.* dispersion in a different medium or uncomplete dispersion.

Treatment A of D42 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, 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 1 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 D2 example 2, which was indicated by the parties as representing the composition of Exjade™) than in a film coated swallowable tablet (1-10%, see paragraph [0011] of the patent).

Moreover, in D42 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 D42 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 respondent during oral proceedings, the tablet "in the form of an oral dosage form" generally disclosed in D9 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. D9 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 D9 nor the results of D42 would have provided a reasonable expectation of success of good bioavailability when formulating deferasirox in film coated swallowable tablets.

3.5.6 As explained by the respondent, the skilled person would furthermore be aware of the fact that SLS may contribute to the dissolution of the tablet of example 26 of D9. 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 be obtained with such a replacement.

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

Order

For these reasons it is decided that:

The appeals are dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated