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Datasheet for the decision of 20 April 2023

Case Number: T 0402/21 - 3.3.07

Application Number: 14727455.9

Publication Number: 3003277

IPC: A61K9/14, A61K9/20, A61K31/5377

Language of the proceedings: EN

Title of invention:
PROCESS FOR THE PREPARATION OF A PHARMACEUTICAL COMPOSITION COMPRISING RIVAROXABAN

Patent Proprietor:
Sandoz AG

Opponent:
HGF Limited

Headword:
Preparation of a rivaroxaban composition / SANDOZ

Relevant legal provisions:
RPBA 2020 Art. 12(2), 13(1), 13(2)
EPC Art. 54, 56

Keyword:
primary object of appeal proceedings to review decision - appeal case directed to objections on which decision was based (yes)
Amendment after summons - taken into account (no)
Novelty - main request and auxiliary request 1 (no)
Inventive step - auxiliary requests 2 to 7 (no)

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Case Number: T 0402/21 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 20 April 2023

Appellant: (Opponent)	HGF Limited 1 City Walk Leeds Yorkshire LS11 9DX (GB)
Representative:	HGF HGF Limited 1 City Walk Leeds LS11 9DX (GB)
Respondent: (Patent Proprietor)	Sandoz AG Lichtstrasse 35 4056 Basel (CH)
Representative:	Maiwald GmbH Elisenhof Elisenstraße 3 80335 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 22 February 2021 concerning maintenance of the European Patent No. 3003277 in amended form.**

Composition of the Board:

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

Summary of Facts and Submissions

I. European patent 3 003 277 (hereinafter "the patent") was granted on the basis of 14 claims. The independent claim of the patent as granted read as follows:

"1. A process for the preparation of a pharmaceutical composition comprising (S)-5-chloro-N-{[2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]oxazolidin-5-yl]methyl} thiophene-2-carboxamide, wherein the process comprises a step of

a) milling a mixture comprising (S)-5-chloro-N-{[2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]oxazolidin-5-yl]methyl}thiophene-2-carboxamide and at least one hydrophilic binder, wherein the mixture further comprises at least one surfactant."

II. An opposition was filed against the patent on the grounds that its subject-matter lacked novelty and inventive step.

III. The opposition division took the interlocutory decision that, on the basis of the main request filed on 17 April 2020 (claims) and during the oral proceedings on 13 January 2021 (amended description pages), the patent met the requirements of the EPC.

IV. The decision of the opposition division, posted on 22 February 2021, cited *inter alia* the following documents:

D1: WO 2010/146179 A2
D4: Barabas and Adeyeye, Analytical Profiles of Drug Substances and Excipients, Vol. 24, 1996, page 90

D5: Vogt *et al.*, European Journal of Pharmaceutics and Biopharmaceutics, 68, (2008), 330-337
D12: Wasilewska and Winnicka, Materials, 12, (2009), 3386, pages 1-21

V. The opposition division decided in particular as follows:

(a) The processes of examples 5, in particular 5-4, and 7 of D1 did not anticipate the subject-matter of the claims of the main request.
(b) The subject-matter of the claims of the main request was not obvious starting from the closest prior art D1.

VI. The opponent (appellant) lodged an appeal against the above decision of the opposition division.

VII. With its reply to the appellant's statement setting out the grounds of appeal the patent proprietor (respondent) defended its case on the basis of the main request maintained during the first instance proceedings (main request), and on the basis of auxiliary requests 1 to 7 filed therewith (wherein auxiliary request 1 corresponded to auxiliary request 1 filed on 14 April 2020, auxiliary requests 2 and 4 corresponded to auxiliary requests 2 and 3 filed on 13 November 2020, and auxiliary requests 5 and 6 corresponded to auxiliary requests 4 and 5 filed on 13 November 2020 being identical to auxiliary requests 3 and 4 filed on 14 April 2020).

The content of the claims upon which the present decision is based can be illustrated as follows:

Claim 1 of the main request read as follows:

"1. A process for the preparation of a pharmaceutical composition comprising (S)-5chloro-N-{[2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]oxazolidin-5yl]methyl} thiophene-2-carboxamide, wherein the process comprises a step of

a) Milling a mixture comprising (S)-5-chloro-N-{[2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]oxazolidin-5-yl]methyl}thiophene-2-carboxamide and at least one hydrophilic binder, wherein the mixture further comprises at least one surfactant and wherein the mixture further comprises at least one filler."

Claim 1 of auxiliary request 1 corresponded to claim 1 of the main request with the feature "wherein step a) is carried out by dry milling" added at the end of the claim.

Claim 1 of auxiliary request 2 corresponded to claim 1 of the main request, wherein the hydrophilic binder was specified as "selected from the group consisting of hydroxypropyl methyl cellulose, cellulose methyl ether, hydroxypropyl cellulose, ethyl cellulose, carboxymethyl cellulose, galactomannan gum, xanthan, glycerides, acrylic and methacrylic copolymers with trimethylammoniomethyl acrylate, copolymers of dimethylaminomethacrylic acid and neutral methacrylic acid esters, polymers of methacrylic acid or methacrylic acid, and any mixtures thereof".

Claim 1 of auxiliary request 3 corresponded to claim 1 of auxiliary request 2, wherein the filler was specified as "selected from the group consisting of lactose, dextrose, maltose, sucrose, glucose, fructose, mannitol, maltitol, sorbitol, xylitol, cellulose powder, microcrystalline cellulose, dicalcium

phosphate, tricalcium phosphate, magnesium trisilicate and any mixtures thereof".

Claim 1 of auxiliary request 4 corresponded to claim 1 of auxiliary request 1, wherein the hydrophilic binder was specified as in auxiliary request 2.

Claims 1 of auxiliary requests 5 and 6 corresponded to claims 1 of the main request and auxiliary request 4 respectively, wherein the feature "wherein the process does not include granulating (S)-5-chloro-N-{[2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]oxazolidin-5-yl]methyl} thiophene-2-carboxamide or granulating a mixture comprising (S)-5-chloro-N-{[2-oxo-3-[4-(3-oxomorpholin-4-yl)phenyl]oxazolidin-5-yl]methyl} thiophene-2-carboxamide" was added at the end of the claim.

Claim 1 of auxiliary request 7 corresponded to claim 1 of auxiliary request 6, wherein the filler was specified as "selected from the group consisting of lactose, dextrose, maltose, sucrose, glucose, fructose, mannitol, maltitol, sorbitol, xylitol, cellulose powder, microcrystalline cellulose, dicalcium phosphate, tricalcium phosphate, magnesium trisilicate and any mixtures thereof".

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

(a) Documents filed by the appellant on 10 May 2022 (D14) and 23 March 2023 (D16):

D14: Textbook "Calcium Phosphates in Biological and Industrial Systems", Chapter 13. "Calcium Phosphate in Pharmaceutical development", 1998

D16: "Croscarmellose sodium" Product information sheet, VIO CHMICALS

(b) Documents filed by the respondent on 7 March 2023:

D2a: Handbook of Pharmaceutical Excipients, 6th edition, 2009 - entries for carboxymethylcellulose sodium, croscarmellose sodium, crospovidone, and povidone
D15: Opinion of Prof. Dr. Wagner with the following annexes:
- Lists of publication of Prof. Dr. Wagner
- CV of Prof. Dr. Wagner
- Textbook Voigt, "Pharmazeutische Technologies" 11th Edition, 2010
- Textbook Liebermann, Lachmann "Pharmaceutical Doasage Forms: Tablets", Vol. 2, 2nd revised Edition, 1990

IX. Oral proceedings were held before the Board on 20 April 2023.

X. The appellant requested that the decision under appeal be set aside and that the patent be revoked.

The appellant also requested that documents D2a and D15, including the annexes to D15, not be admitted into the appeal proceedings. Should document D2a be admitted, then the appellant requested to admit into the appeal proceedings the document D16.

Finally the appellant requested the arguments of the respondent presented in the letter dated 7 March 2023 regarding the interpretation of the terms "mixture" and "milling" and relating to croscarmellose not be admitted into the appeal proceedings.

XI. The respondent requested that the appeal be dismissed and 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 1-7 filed with the reply to the statement of the grounds of appeal.

The respondent further requested the novelty attack over example 5-4 of D1 made with the statement of the grounds of appeal not be admitted into the appeal proceedings.

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

(a) The objection of lack of novelty over example 5-4 of D1 raised in the statement setting out the grounds of appeal was not to be disregarded since it had already been raised and maintained during the opposition proceedings.

(b) In its submission of 7 March 2023, the respondent provided for the first time new arguments relating to the interpretation of "mixture" and "milling" and filed D15 in connection thereto. These submissions constituted amendments to the respondent's case, which were not to be admitted into the appeal proceedings.

(c) The same applied *mutatis mutandis* to the new arguments concerning croscarmellose and D2a provided by the respondent with the same submission of 7 March 2023, which were also not to be admitted into the appeal proceedings.

(d) The process of example 5-4 of D1 anticipated the process of claim 1 of the main request. Crospovidone was indeed known as being hydrophilic and having binder properties. The operation of milling into granules of this example was furthermore encompassed by the scope of claim 1 of the main request.

(e) The subject-matter of claim 1 of auxiliary request 1 was also not novel over example 5-4 of D1 since the additional feature of dry milling was disclosed therein.

(f) Document D1 represented the closest prior art. The subject-matter of claim 1 of auxiliary request 2 differed from the process of example 5A-3 of D1 in that the mixture subjected to milling additionally contained a hydrophilic binder and a surfactant. No particular effect linked thereto had been substantiated. The objective technical problem, as formulated during the oral proceedings, resided in the provision of an alternative simple and economical process for the preparation of a pharmaceutical composition comprising rivaroxaban and having satisfactory dissolution properties. Performing a milling with further excipients, including binders and surfactants, was generally suggested in D1. D1 further disclosed some of the presently claimed specific binders. Auxiliary request 2 did thus not meet the requirements of Article 56 EPC.

(g) Auxiliary requests 3 to 7 did not fulfill the requirements of Article 56 EPC for similar reasons as for auxiliary request 2, because the features introduced in the claims 1 of these auxiliary

requests compared to the main request were already either disclosed in example 5A-3 of D1 or generally taught in D1.

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

(a) The objection of lack of novelty over example 5-4 of D1 was newly raised and should not be admitted into the appeal proceedings.

(b) The arguments provided in the letter of 7 March 2023 and supported by D15 relating to the interpretation of the terms "milling" and "mixture" did not represent amendments to the case but constituted further evidence of how these terms were to be interpreted in reply to the preliminary opinion of the Board. Moreover these submissions would not add complexity to the case. They were thus to be admitted into the appeal proceedings.

(c) The arguments provided in the letter of 7 March 2023 relating to croscarmellose and D2a aimed merely at clarifying the common general knowledge regarding some excipients and their functions in reply to the preliminary opinion of the Board. These arguments as well as D2a were thus to be admitted into the appeal proceedings.

(d) The process of claim 1 of the main request was novel over the one of example 5-4 of D1. Crospovidone did indeed not represent a hydrophilic binder according to the patent. Moreover, the claimed step of milling of a mixture would not be understood by a skilled person as the milling of a compact or granules.

(e) The process of claim 1 of auxiliary request 1 was novel for the same reasons as the main request.

(f) Document D1 represented the closest prior art. The subject-matter of claim 1 of auxiliary request 2 differed from the process of example 5A-3 of D1 in that the mixture subjected to milling additionally contained a hydrophilic binder and a surfactant. Even if the objective technical problem was considered as the provision of an alternative simple and economical process for the preparation of a pharmaceutical composition comprising rivaroxaban and having satisfactory dissolution properties, the process defined in claim 1 of auxiliary request 2 would constitute a non-obvious solution thereto. D1 did indeed not provide any pointer towards the milling of the particular combination of rivaroxaban with the three types of excipients claimed, let alone with the aim of obtaining satisfactory dissolution properties. Auxiliary request 2 did thus fulfill the requirements of Article 56 EPC.

(g) Auxiliary requests 3 to 7 met the requirements of Article 56 EPC for the same reasons as auxiliary request 2.

Reasons for the Decision

1. Admittance of objections, new arguments and new items of evidence

1.1 Objection of lack of novelty based on example 5-4 of D1

1.1.1 The respondent argued that the objection of lack of novelty over example 5-4 of D1 of the appellant was newly raised in the statement setting out the grounds of appeal and should thus not be admitted into the appeal proceedings.

1.1.2 The Board observes that an objection of lack of novelty of the granted claim over example 5, including examples 5-1 to 5-5, was already raised by the appellant in the notice of opposition (see page 3 item 13 of the notice). This objection was maintained against the amended main request in the letter of the appellant of 12 November 2020 (see items 19-25 of this letter). This objection relied on the argument that the claims in suit did not exclude that the mixture subjected to milling was a granulated mixture. The novelty of claim 1 of the main request over example 5 of D1, including examples 5-1 to 5-5, was furthermore extensively discussed in the impugned decision (see page 6 items 3.3 to 3.7 of the impugned decision). Finally, the respondent has not identified any particular new argument in support of this objection, which would not have been already raised during the first instance proceedings.

1.1.3 The present objection has therefore been already raised and maintained during the whole opposition proceedings. Accordingly, there is no reason to exclude this

objection from the appeal proceedings (Article 12(2) RPBA 2020).

1.2 New arguments concerning the terms "milling" and "mixture" and document D15

1.2.1 In the letter dated 7 March 2023, *i.e.* after notification of the summons to oral proceedings (dated 27 June 2022), the respondent provided further arguments concerning the interpretation of the terms "mixture" and "milling" in claim 1 of the main request. These arguments related to the "intention", *i.e.* the scope, linked to the milling step in the patent, which would reside in a particle size reduction of the active ingredient and not of granules. Furthermore, the respondent provided the declaration D15 in support thereof.

1.2.2 According to the respondent, these arguments would represent a mere clarification of the manner in which the respondent interpreted the terms "milling a mixture" throughout the proceedings and would thus not result in the presentation of any new matter.

Furthermore, the preliminary opinion of the Board constituted the first opinion of a body of the EPO not following the respondent's interpretation. Document D15 had been filed in reaction thereto. An earlier filing of document D15 would not have been required, because there was no indication before that the interpretation of the appellant would ever be followed by a skilled person.

1.2.3 The Board observes that the arguments relating to the "intention" of mixing and milling processes and to the particle size reduction had never been provided before

in the appeal procedure, while the issue of interpretation of the terms "milling a mixture" in the claims was a key point in the impugned decision and the statement setting out the grounds of appeal. They do therefore constitute an amendment to the case of the respondent (Article 12(4) RPBA 2020). Their admittance as well as the one of document D15 is thus to be assessed according to Articles 13(1) and (2) RPBA 2020.

1.2.4 The interpretation of these terms in the preliminary opinion of the Board was based on arguments and passages of the patent (*i.e.* paragraph [0019] and claim 12) mentioned by the appellant. Hence, this preliminary opinion cannot be considered to provide exceptional circumstances in the sense of Article 13(2) RPBA 2020.

1.2.5 Moreover, claim 1 of the main request does not define any particular particle size reduction of any particular component beyond the one generally encompassed by the term "milling" as commonly understood *i.e.* as being applied to any "material" as defined in paragraph [0010] of the patent. The newly provided arguments as well as D15 do therefore not appear suitable to resolve the novelty or inventive step issues underlying the present case (Article 13(1) RPBA 2020).

1.2.6 Accordingly, the new arguments of the respondent submitted in the letter dated 7 March 2023 concerning the terms "mixture" and "milling" as well as document D15 are not admitted into the appeal proceedings (Articles 13(1) and 13(2) RPBA 2020).

1.3 New arguments concerning croscarmellose and document D2a

1.3.1 In the letter dated 7 March 2023, *i.e.* after notification of the summons to oral proceedings (dated 27 June 2022), the respondent provided arguments on croscarmellose in relation to the objection of lack of novelty over example 5-5 of D1. The respondent explained that, as commonly known, croscarmellose would be a cross-linked carboxymethylcellulose being thus different from the product carboxymethylcellulose *per se*. It could thus not be understood as generally encompassed by the term "carboxymethylcellulose" used in the patent. Furthermore carboxymethylcellulose could not be considered as a binder. D2a, containing the entries for carboxymethylcellulose sodium and croscarmellose sodium of the Handbook of Pharmaceutical excipients, was filed in support of these arguments.

1.3.2 According to the respondent, these arguments and document D2a provided merely clarification of common general knowledge regarding croscarmellose and its functions in reply to the preliminary opinion of the Board. Furthermore it had always been the position of the respondent that croscarmellose was not a binder. This was apparent from the reference in the patent in suit to croscarmellose as a disintegrant. These arguments as well as D2a were thus to be admitted into the appeal proceedings.

1.3.3 The Board notes that the respondent argued for the first time in the letter dated 7 March 2023 that croscarmellose was (i) not to be understood as encompassed by the general term "carboxymethylcellulose" and (ii) not a binder. Its reply to the objection of the appellant over example

5-5 of D1 in its sole previous submission in the appeal proceedings, namely the reply to the statement of the grounds of appeal, was indeed exclusively directed to the absence of a milling step according to claim 1. In addition, the fact that the patent mentioned croscarmellose as a suitable disintegrant cannot be considered as an evidence that croscarmellose would not also act as a binder, let alone as an argument of the respondent in that respect.

It follows that these arguments constitute an amendment to the case of the respondent (Article 12(4) RPBA 2020). Their admittance as well as the one of document D2a is thus to be assessed according to Articles 13(1) and (2) RPBA 2020.

1.3.4 The preliminary opinion of the Board considering croscarmellose in example 5-5 of D1 as a binder merely followed the argument of the appellant as raised in the statement setting out the grounds of appeal. Hence, this preliminary opinion cannot be considered to provide exceptional circumstances in the sense of Article 13(2) RPBA 2020.

1.3.5 Moreover, the indication that croscarmellose is not carboxymethylcellulose *per se* but a cross-linked form thereof does indeed form part of common general knowledge. It does however not appear suitable to resolve the issue of lack of novelty over example 5-5 (Article 13(1) RPBA 2020), since it does not teach that croscarmellose does not function as a binder. The same applies to the fact that the entry for croscarmellose in D2a does not mention that it may function as a binder.

The same applies also to the entries regarding crospovidone and povidone in document D2a, which indeed represent common general knowledge. However they do not provide evidence that crospovidone would not act as a binder, especially since there is further evidence on file which substantiate this function (see D4).

1.3.6 Hence, the new arguments of the respondent submitted in the letter dated 7 March 2023 relating to croscarmellose and document D2a are not admitted into the appeal proceedings (Articles 13(1) and (2) RPBA 2020). As document D16 had been conditionally filed in reply to document D2a, document D16 is not admitted either.

Main request

2. Novelty

2.1 The appellant contested that the subject-matter of claim 1 of the main request would be novel over example 5-4 of document D1.

As argued by the appellant, example 5-4 of document D1 discloses the preparation of tablets comprising *inter alia*:
- rivaroxaban,
- sodium lauryl sulfate, which is a surfactant according to page 7 lines 25-26 of D1,
- calcium hydrogenphosphate, which is a filler according to page 4 lines 25 to 34 of D1, and
- crospovidone, which functions as a binder according to D4 (see page 90, Introduction).

The process of preparation of the tablets of example 5 includes the mixing of rivaroxaban with the above

listed excipients, the dry-granulation of the obtained mixture with a roller-compactor and a step of milling the obtained compact into granules.

2.2 Crospovidone

2.2.1 The respondent argued that crospovidone would not act as a binder in example 5-4 of document D1, because document D1 did not disclose crospovidone in the list of suitable binders but as a disintegrant.

2.2.2 However, as mentioned by the appellant, document D4 substantiates that crospovidone was commonly known as a binder in addition to a disintegrant (see D4, page 90 "Introduction").

2.2.3 During oral proceedings, the respondent further contested that crospovidone would correspond to a hydrophilic binder according to the patent. Crospovidone was indeed known as being water-insoluble as substantiated by document D1 (see crospovidone in the list of "water-insoluble filler" on page 5 line 27 of D1). According to the patent, a hydrophilic compound could be wetted and dissolved (see paragraphs [0011] and [0013] of the patent), which thus required a water-soluble compound.

2.2.4 This argument is not convincing.

2.2.5 According to the patent a "hydrophilic material" refers to "a material having a tendency to be solvated by water. Moreover, it may refer to a material that is attracted to, and tends to be dissolved by water and/or it may refer to a material that has an affinity for water; readily absorbing or dissolving in water." (see paragraph [0011], emphasis added). The patent further

specifies a "hydrophilic binder" as "a material which after inclusion in a formulation increases the rate at which the particle separate, enhancing the available surface area so that wetting and dissolution can occur more rapidly, shortening the time needed for some poorly soluble drugs to go into solution." (see paragraph [0013], emphasis added).

Crospovidone, as a disintegrant (which was not disputed by the respondent), is known to have an ability to uptake water, swell and thus favour particle separation. These properties actually correspond to those mentioned in the above passages of the patent.

2.2.6 Furthermore, as argued by the appellant, the fact that cross-linking renders crospovidone water-insoluble compared to povidone, does not mean that the hydrophilic character of povidone is also lost due to cross-linking. Moreover, as further underlined by the appellant, ethylcellulose which is known as being water-insoluble (see D12) is listed as a suitable hydrophilic binder in the patent (see claim 3 of the patent). Contrary to the opinion of the respondent, it cannot therefore be concluded that the definition of "hydrophilic binder" in the patent excludes any materials which are water-insoluble.

2.2.7 In the absence of any evidence of the contrary, the Board therefore considers it credible that crospovidone corresponds to a hydrophilic binder as defined in the patent.

2.2.8 The tablets according to example 5-4 of document D1 therefore contain all the components defined in present claim 1.

2.3 Milling a mixture

2.3.1 The respondent further argued that the skilled person would not understand the mixture of claim 1 as any kind of mixture of the listed components but would on the contrary consider said mixture as the direct result of mixing the components *i.e.* without any further processing. This would be evident to the skilled person due to the association of the terms "milling" and "mixture". Both terms had to be read together. In this context, the definition of the term "milling" provided in paragraph [0010] would stipulate the obtention of a powder. Furthermore the patent (see paragraph [0019]) would teach that step a) excludes any granulation. The subject-matter of claim 1 would thus not encompass milling a compact. The milling step of example 5-4 would thus not anticipate present step a).

2.3.2 The Board observes that there is no particular commonly recognised meaning for the term "mixture" in the field of pharmaceutical preparation. This can be illustrated by D1, in which a granulated mixture is referred to as a "mixture", see example 5A "Alternative mode of preparation 2", last sentence.

2.3.3 Furthermore the patent does not provide for any specific restricted definition of the terms "mixture" or "milling" or the expression "milling a mixture".

(a) The claim wording *per se* does not limit in any manner the nature of the mixture or the milling step performed. Neither the result of a direct mixing of the components nor a specific isolated co-milling step leading to a powder is defined.

(b) The description does not provide any general definition of the term "mixture".

(c) Contrary to the respondent's view, the definition of the term "milling" in paragraph [0010] does not limit its scope to any particular meaning. Indeed paragraph [0010] first states that this term "as used herein shall be understood as known in the art", *i.e.* as reducing the size of a material, including milling into granules as disclosed in example 5 of D1. It is then specified in paragraph [0010] that "in particular, it shall be understood as an operation in which material is crushed, pulverized, or reduced to powder by friction, especially by rubbing between two hard surfaces" (emphasis added). The use of the term "in particular" renders the described embodiment merely illustrative and without any restrictive effect on the definition of the term milling.

(d) Regarding the argument of the respondent with respect to the obtention of a powder, the Board considers that the terms "reduced to powder by friction" in the sentence "...in which material is crushed, pulverized or reduced to powder by friction" (paragraph [0010]), have to be read together as one expression. It does not appear that the sentence could be read as suggested by the respondent during the oral proceedings such that "crushed", "pulverized" or "reduced" are alternatives to each other all leading to a powder. Indeed, in such a case, the term "by friction" would also have to apply to all three ways of milling, which does not appear logical for crushing and pulverizing.

(e) Moreover the mention of the broad term "material" in paragraph [0010] makes clear that the milling step is not to be performed on any particular type of mixture.

2.3.4 Finally, contrary to the opinion of the appellant, the description of the patent does not generally exclude the mixture being in the form of granules nor step a) being part of a granulation process. To support its position the appellant referred to paragraph [0019] in which it is explained that rivaroxaban "is simply milled together with a hydrophilic binder instead of being granulated". In this regard the Board observes the following.

(a) Paragraph [0019] of the patent in suit refers to the milling of rivaroxaban with merely a hydrophilic binder. There is no mention in this paragraph of performing the milling with further additional excipients, let alone specifically with a surfactant and a filler. Contrary to the respondent's view, the fact that this embodiment was representative of the original independent claim does not mean that it necessarily applies to the amended claim, in particular as the components of the mixture have been amended. It remains therefore ambiguous whether this embodiment is directly representative of the process presently claimed.

(b) Moreover, as explained by the appellant during the oral proceedings, the particular embodiment of paragraph [0019] relating to milling in contrast to granulation can be interpreted as merely representing one advantageous embodiment offered by the invention (the term "allows" has no restrictive

meaning), which does thus not limit the scope of claim 1.

(c) Furthermore, present dependent claim 12 specifies, as a sub-embodiment of the subject-matter of present claim 1, a process which does not include granulating rivaroxaban or granulating a mixture comprising rivaroxaban. The Board considers that this dependent claim implies that granules were not excluded from the mixture mentioned in independent claim 1.

The respondent argued that dependent claim 12 would not be in contradiction with the exclusion of any granulation at step a) already in claim 1. It would merely aim at disclaiming granulation at any and all stages of the entire process. Thus granulation after step a) being permitted in claim 1 would no longer be permitted under claim 12. The Board cannot identify any basis for such a limited interpretation. As detailed above, the patent does not provide any support for a limited interpretation of claim 1.

2.3.5 In this context, a large part of the respondent's argumentation concentrated on the difference between the core part of the patent represented by the examples and example 5-4 of D1 as well as on the "intention" of the milling step according to the patent. The Board agrees that the physical state of the mixture and the milling step of the examples of the patent (see example 1) differ from those of example 5-4 of D1. However, the scope of present independent claim 1 cannot be limited to the core "intention" of the patent embodied in the examples. In the present case, the entire scope of claim 1, independently of the core "intention" of the

patent, has to be taken into account when assessing the issue of novelty.

2.3.6 The Board therefore considers that claim 1 of the main request does not contain any feature that would distinguish the claimed milling step from the one of example 5-4.

2.4 Accordingly, the main request is not novel over document D1 (Article 54 EPC).

Auxiliary request 1

3. Novelty

3.1 Compared to claim 1 of the main request, claim 1 of auxiliary request 1 contains the further feature "wherein step a) is carried out by dry milling".

3.2 As stated by the appellant, example 5-4 of D1 is performed by dry granulation, *i.e.* the milling step is a dry milling step.

3.3 The respondent did not provide any specific argument why auxiliary request 1 would overcome the lack of novelty finding for the main request.

3.4 As a result, the additional feature introduced in claim 1 of auxiliary request 1 is already disclosed in example 5-4 of D1 and the reasoning developed for claim 1 of the main request under point 2. applies *mutatis mutandis* to claim 1 of auxiliary request 1. Hence, auxiliary request 1 is not novel over document D1 (Article 54 EPC).

Auxiliary request 2

4. Novelty

Claim 1 of auxiliary request 2 corresponds to claim 1 of the main request wherein the hydrophilic binder was limited to the list of specific binders of granted claim 3. The appellant did not raise any objection of lack of novelty for auxiliary request 2.

5. Inventive step

5.1 The patent in suit relates to a simpler and more economical process for the preparation of a pharmaceutical composition comprising rivaroxaban and having a satisfactory solubility and dissolution rate in water (see paragraphs [0001] and [0007] of the patent). The claimed process comprises a step of milling a mixture containing rivaroxaban, a surfactant, a filler and a hydrophilic binder.

5.2 During oral proceedings both parties considered D1 as representing the closest prior art. In particular, example 5A-3 was considered as starting point by the appellant, which was not contested by the respondent.

D1 relates to the same purpose as the patent in suit, namely the provision of an economical and simpler process (see page 3 lines 5 to 10). It discloses compositions comprising rivaroxaban in combination with a surfactant, a filler and a binder (see claim 14, page 9 line 36 to page 10 line 26, Examples 5-1 to 5-5 or 6A-1 to 6A-4) as well as the co-milling of rivaroxaban and a filler (see claim 12 and examples 5A1-5A5). Example 5A-3 discloses the co-milling of rivaroxaban with a filler (lactose monohydrate) and the subsequent

addition of a hydrophilic binder (microcrystalline cellulose) in the composition. However the composition does not contain a surfactant.

5.3 The process of present claim 1 differs from the process of example 5A-3 in that the mixture subjected to milling contains, in addition to rivaroxaban and a filler, also a hydrophilic binder and a surfactant (the latter not being contained in the composition of example 5A-3 at all).

5.4 During the oral proceedings, the respondent did not pursue its argument regarding an improved property of the claimed process (namely leading to compositions having superior dissolution properties).

The Board maintains its view expressed in its preliminary opinion (see item 3.4.2) that no improved dissolution properties have been substantiated compared to the compositions obtained *via* the processes of D1, let alone over the whole scope of the claims. The patent does indeed not contain any comparative example, which would substantiate an effect of the distinguishing feature compared to the closest prior art process of D1. A comparison of the dissolution properties of the compositions obtained by the present process and the one of example 5A-3 of D1 by means of an intermediate comparison of each of those compositions to Xarelto is also not possible because no detailed dissolution data are available for the composition obtained in example 5A-3 of D1, apart from the general statement that the compositions of D1 are at least comparable to Xarelto. Finally, regarding the achievement of an effect over the whole scope of the claims, the data of figure 2 of the patent indicate that an improved dissolution profile compared to

Xarelto is not achieved by all the compositions obtained by the claimed process.

Accordingly, it can only be considered that the claimed process leads to compositions with satisfactory dissolution properties.

5.5 It follows that, starting from example 5A-3 of D1, the objective technical problem resides in the provision of an alternative simple and economical process for the preparation of a pharmaceutical composition comprising rivaroxaban and having satisfactory dissolution properties. This formulation was not disputed by the parties during oral proceedings.

5.6 The Board observes that it is stated on page 10 lines 28 to 31 of D1 that "compositions according to the previous embodiment" (*i.e.* compositions containing rivaroxaban and all presently claimed excipients) are particularly suitable to be prepared *inter alia* by co-milling. This passage is general and does not limit the number and nature of the components to be co-milled. This passage therefore generally encompasses the presently claimed subject-matter.

Furthermore D1 mentions on page 15 lines 4 to 5 that "preferably, the rivaroxaban is co-milled with at least one hydrophilic excipient" and the suitable hydrophilic excipients listed immediately after on page 15 lines 5 to 9 correspond to fillers. A co-milling with copovidone (which is commonly known as a hydrophilic binder) and a surfactant is furthermore also envisaged on page 15 line 11 to 13. It follows that the skilled person would understand from D1 that any of these excipient classes, namely filler, binder and surfactant, may be co-milled with rivaroxaban. This

constitutes a pointer towards which types of excipients disclosed in the general embodiment of page 10 are suitable for milling with rivaroxaban.

Moreover, several of the presently claimed hydrophilic binders are disclosed in the list of suitable binders in D1 (see page 6 of D1).

Finally, as the compositions of D1 are described as exhibiting a dissolution profile at least comparable to known rivaroxaban formulations (see page 12 lines 26-32 of D1), any composition obtained by a process according to D1 would be expected, in the absence of any indication of the contrary, to have satisfactory dissolution properties.

As a result, in the absence of any particular effect, the process of claim 1 constitutes one out of several equally suggested alternatives in D1.

5.7 The respondent argued that D1 would not provide any pointer to the combination of features of present claim 1, namely the milling of rivaroxaban with not only a filler but also a hydrophilic binder and a surfactant. The cited embodiments disclosed on page 15 would define two alternative embodiments: the co-milling of rivaroxaban with a filler on the one hand and the co-milling of rivaroxaban with copovidone and a surfactant on the other hand. This would not provide a hint to the present combination of excipients. Also the passage on page 10 would not provide such a hint, because several features would have to be selected to arrive at the presently claimed subject-matter. Finally there would be no indication in D1 that every single possible combination within the very general disclosure thereof would be expected to lead to compositions with

satisfactory dissolution properties. Hence, the skilled person would not have arrived at the subject-matter of claim 1 of auxiliary request 2 without hindsight.

5.8 This argument is not convincing. For the reasons detailed above, the Board considers that there are pointers towards the selection of the type of excipients to be milled together with rivaroxaban. The requirement that a pointer towards a particular selection must be present in the prior art for the selection to lack inventive step cannot be considered, in the present case, as necessitating the disclosure in a separate embodiment of the milling of the exact combination of the three types of excipients presently claimed with rivaroxaban. For the assessment of the issue of inventive step, the skilled person is not devoid of any skills but has average knowledge and abilities in the field allowing in the present case the identification of the pointers detailed above.

5.9 In its written submissions, the respondent also referred to D5 as allegedly providing a teaching away from co-milling with a surfactant. In the letter dated 7 March 2023, the respondent also stated that D5 would highlight the difficulty in predicting the dissolution properties of a composition since the addition of a surfactant in the co-milling step led to a lower final solubility. The Board however considers that the actual data provided in D5 do not teach away from milling rivaroxaban with *inter alia* a surfactant. First and foremost because D5 does not relate to rivaroxaban. Furthermore because the provided data only appear to show that no supersaturation occurs when a surfactant is added to the co-milled mixture, which does not allow any conclusion about the actual dissolution profile of

a dosage form obtained by a process involving such a co-milling.

5.10 Thus, auxiliary request 2 does not comply with the requirement of inventive step (Article 56 EPC).

Auxiliary requests 3 to 7

6. Inventive step

6.1 The following features were introduced in claims 1 of auxiliary requests 3 to 7 compared to the main request:

(a) specific list of binders as in auxiliary request 2 (auxiliary requests 3, 4, 6 and 7)
(b) specific list of fillers which includes lactose (auxiliary requests 3 and 7),
(c) step a) being carried out by dry milling as in auxiliary request 1 (auxiliary requests 4, 6 and 7), and /or
(d) the process does not include granulating rivaroxaban or granulating a mixture comprising rivaroxaban (auxiliary requests 5, 6 and 7).

6.2 Feature (a) is not considered to render the claimed subject-matter inventive for the reasons provided for auxiliary request 2 (see point 5.).

6.3 Features (b), (c) and (d) do not represent a further distinguishing feature compared to the closest prior example 5A-3, since lactose (feature (b)) is used as filler in said example, the milling step in said example is a dry milling (feature (c); see page 26 line 12 together with page 4 lines 3 to 5 of D1) and in the alternative mode of preparation 1 of example 5A no granulation takes place (feature (d)).

6.4 Furthermore, the respondent did not provide any specific argument why auxiliary requests 3 to 7 would overcome the lack of inventive step finding for auxiliary request 2.

6.5 Accordingly, the reasoning developed for auxiliary request 2 under point 5. applies *mutatis mutandis* to auxiliary requests 3 to 7. Hence, auxiliary requests 3 to 7 do not meet the requirements of Article 56 EPC.

Order

For these reasons it is decided that:

The decision under appeal is set aside.

The patent is revoked.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated