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Datasheet for the decision of 21 May 2021

Case Number: T 0414/18 - 3.3.07

Application Number: 11791161.0

Publication Number: 2640362

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Language of the proceedings: EN

Title of invention:
THERAPEUTIC COMPOSITIONS COMPRISING RILPIVIRIN HCL AND TENOVOFIR DISOPROXIL FUMARATE

Patent Proprietor:
Gilead Sciences, Inc.
Janssen Sciences Ireland UC

Opponents:
LEK Pharmaceuticals d.d.
HGF Limited

Headword:
Compositions comprising rilpiverin/GILEAD

Relevant legal provisions:
EPC Art. 56, 84, 54, 87

Keyword:

Inventive step - effect not made credible within the whole scope of claim - Main request and auxiliary requests 2, 4, 6-8, 10, 11 - auxiliary request 12 (yes)
Claims - clarity after amendment (no) - auxiliary requests 1, 3, 5, 9 - clarity after amendment (yes) - auxiliary request 12
Novelty - public prior use (no)

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Case Number: T 0414/18 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 21 May 2021

Appellant: (Patent Proprietor 1)	Gilead Sciences, Inc. 333 Lakeside Drive Foster City, CA 94404 (US)
Appellant: (Patent Proprietor 2)	Janssen Sciences Ireland UC Eastgate Village, Eastgate Little Island, County Cork (IE)
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Party as of right: (Opponent 2)	HGF Limited Belgrave Hall Belgrave Street Leeds LS2 8DD (GB)
Representative:	HGF 1 City Walk Leeds LS11 9DX (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on**

29 November 2017 concerning maintenance of the European Patent No. 2640362 in amended form.

Composition of the Board:

Chairman	A. Usuelli
Members:	M. Steendijk
	A. Jimenez

Summary of Facts and Submissions

I. European patent 2 640 362 (hereinafter "the patent") was granted on the basis of twenty three claims.

Independent claim 1 as granted related to:

"A tablet comprising a first layer and a second layer wherein; a) the first layer comprises rilpivirine HCl and is substantially free of tenofovir disoproxil fumarate, and wherein less than about 12.2 weight percent of the first layer is rilpivirine HCl; b) the second layer comprises tenofovir disoproxil fumarate and is substantially free of rilpivirine HCl; and c) the tablet further comprises emtricitabine."

Dependent claim 15 as granted defined in its second embodiment the first layer of the tablet to consist of:

Ingredient	Unit Formula for Tablets (mg/tablet)
Rilpivirine HCl	27.5
Microcrystalline Cellulose	60.0
Lactose Monohydrate	189.8
Povidone	3.3
Polysorbate 20	0.4
Croscarmellose Sodium	16.1
Magnesium Stearate	3.0

and the second layer to consist of:

Ingredient	Unit Formula for Tablets (mg/tablet)
Emtricitabine	200.0
Tenofovir disoproxil fumarate	300.0
Microcrystalline Cellulose	150.0
Lactose Monohydrate	80.0
Pregelatinized Starch	50.0
Croscarmellose Sodium	60.0
Magnesium Stearate	10.0.

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

The appeals filed by the patent proprietors and opponent 1 lie against the interlocutory decision of the opposition division that the patent as amended in accordance with auxiliary request 6 was found to meet the requirements of the EPC.

The decision of the opposition division was based on the main request and auxiliary requests 1-4, all filed on 14 July 2017, and auxiliary requests 5 and 6 filed during the oral proceeding on 14 September 2017.

Claim 1 of the main request related to:

"A tablet comprising a first layer and a second layer wherein the first layer consists of:

Ingredient	%w/w	Unit Formula for Tablets (mg/tablet)
Rilpivirine HCl	2.4	27.5
Microcrystalline Cellulose	5.2	60.0
Lactose Monohydrate	16.5	189.8
Povidone	0.3	3.3
Polysorbate 20	0.03	0.4
Croscarmellose Sodium	1.4	16.1
Magnesium Stearate	0.3	3.0

and the second layer consists of:

Ingredient	% w/w	Unit Formula for Tablets (mg/tablet)
Emtricitabine	17.4	200.0
Tenofovir disoproxil fumarate	26.1	300.0
Microcrystalline Cellulose	13.0	150.0
Lactose Monohydrate	7.0	80.0
Pregelatinized Starch	4.3	50.0
Croscarmellose Sodium	5.2	60.0
Magnesium Stearate	0.9	10.0

"

Dependent claim 2 defined:

"The tablet of claim 1 further comprising a third layer that is between and separates the first and second layer, wherein the third layer comprises 150 ± 8.0 mg of microcrystalline cellulose or lactose monohydrate, or a mixture thereof."

Dependent claim 3 defined:

"The tablet of claim 1 or claim 2 that further comprises a film coating"

III. The following documents were *inter alia* cited in the decision under appeal:

D1: WO 2005/021001
D3: WO 2006/135932
D6: Mathias et al., XVIII International AIDS Conference, 2010,XP009151551
D10: Press of release of Gilead Sciences 10.08.2011
D23: Press release of Gilead Sciences 23 09.2011
D31: "Die Tablette", Ritschel et al., 2nd edition, 2002, 23
D33: ATRIPLA® EPAR Scientific Discussion 19.12.2007
D37: EP 1 632 232 A1
D43: US2009/0143314

IV. The opposition division came to the following conclusions:

(a) Claim 1 as amended in accordance with the main request lacked clarity due to a contradiction, as this independent claim defined a tablet in an open manner, allowing additional components such as defined in dependent claim 2, and at the same time defined specific components of the tablet that already reached a total sum of 100% w/w.

The contradiction persisted in auxiliary requests 1-5.

(b) The claims of auxiliary request 6 met the requirements of Article 84 EPC.

(c) The subject-matter of auxiliary request 6 was sufficiently disclosed in the patent having regard to the exemplified preparation method.

(d) The subject-matter of auxiliary request 6 was entitled to the claimed priority of 19 November 2010.

(e) The COMPLERA / EVIPLERA product was according to documents D10 and D23 approved by the FDA on 10 August 2011, which was after the effective date for the patent. No evidence of any public use of these products prior to the effective date of 19 November 2010 resulted from the documents on file.

(f) Document D6 represented the closest prior art describing a triple combination tablet containing rilpivirine, emtricitabine and tenofovir disoproxil fumarate. The subject-matter of claim 1 of auxiliary request 6 differed from the tablet of document D6 in the definition of the bilayer structure and the specific excipient components.

In view of the pharmacokinetic profile presented for formulation 3 in example 5 of the patent the problem to be solved was seen in the provision of a formulation showing bioequivalence to separate tablets of the active agents.

The determination of the appropriate excipients and their amounts was not a matter of obviousness having regard to the effects of even small variations in the amounts of excipients on the pharmacokinetics.

No different conclusion would be reached starting from document D1, which also referred to a triple combination tablet for the defined active agents.

V. With the statement setting out the grounds of appeal the appellant-patent proprietor filed its main request and auxiliary requests 1-13.

The claims of the main request corresponded to the claims of the main request on which the decision under appeal was based.

The claims of auxiliary request 1 corresponded to the claims of the main request, except that claim 1 defined the tablet as "consisting of a first layer and a second layer ...".

The claims of auxiliary request 2 corresponded to the claims of the main request, except that claim 2 was deleted.

The claims of auxiliary request 3 corresponded to the claims of the main request, except that claim 1 defined the tablet as "consisting of a first layer and a second layer ..." and that claim 2 was deleted.

The claims of auxiliary request 4 corresponded to the claims of the main request, except that claim 3 was reformulated as an independent claim to define:

"A film coated tablet wherein the film coated tablet comprises the tablet as defined in claim 1 or claim 2 and a film coating that covers a portion or all of the tablet."

The claims of auxiliary request 5 corresponded to the claims of auxiliary request 4, except that claim 1 defined the tablet as "consisting of a first layer and a second layer ...".

The claims of auxiliary request 6 corresponded to the claims of auxiliary request 4, except that claim 2 was deleted.

The claims of auxiliary request 7 corresponded to the claims of auxiliary request 4, except that claim 1 defined the tablet as "consisting of a first layer and a second layer ..." and that claim 2 was deleted with the consequence that claim 3 of auxiliary request 4 (see above) became claim 2 in auxiliary request 7.

The claims of auxiliary request 8 corresponded to the claims of the main request, except that claim 3 was deleted.

The claims of auxiliary request 9 corresponded to the claims of the main request except that claim 1 defined the tablet as "consisting of a first layer and a second layer ..." and that claim 3 was deleted.

The claims of auxiliary request 10 corresponded to the claims of main request except that claims 2 and 3 were deleted.

The claims of auxiliary request 11 corresponded to the claims of the main request except that claim 1 defined the tablet as "consisting of a first layer and a second layer ..." and that claims 2 and 3 were deleted.

The claims of auxiliary request 12 corresponded to the claims of the main request except that claim 1 defined the tablet as "consisting of a first layer and a second layer, optionally a third layer that is between and separates the first and second layer, and optionally a film coating,..." with the further

definition "and the optional third layer consists of 150 ± 8.0 mg of microcrystalline cellulose or lactose monohydrate, or a mixture thereof" and that claims 2 and 3 were deleted.

The claims of auxiliary request 13 corresponded to the claims of the main request, except that the tablet was defined as "consisting of a first layer and a second layer, and optionally a film coating, ..." and that claims 2 and 3 were deleted.

The claims of auxiliary requests 1, 3, 8, 9, 7 and 11 corresponded respectively to the claims of auxiliary requests 1-6 on which the decision under appeal was based.

VI. With the statement setting out the grounds of appeal the appellant-opponent 1 submitted the following documents:

D44: R. Voigt "Pharmazeutische Technologie", 2006, 219-220
D45: EMEA Guideline on the investigation of Bioequivalence, 2010
D46: Mathias et al., J Bioequiv. Availab. 2012, 4:7, 100-105

VII. The appellant-patent proprietors objected to the filing of documents D44-D46 with their reply of 22 August 2018.

The appellant-opponent 1 objected to the filing of the new auxiliary requests 2, 4, 5, 6, 10, 12 and 13 with its reply of 21 August 2018.

VIII. The Board issued a communication pursuant to Article 15(1) RPBA on 11 November 2020.

IX. With the consent of the parties oral proceedings were held on 21 May 2021 in the form of a videoconference. The oral proceedings were attended by the appellant-patent proprietor and the appellant-opponent 1. The respondent-opponent 2 had announced not to attend.

During the oral proceedings the appellant-patent proprietors promoted the previously filed auxiliary request 13 to the rank of auxiliary request 11 and renumbered the subsequent requests accordingly.

X. The arguments of the appellant-patent proprietors in as far as relevant to the present decision can be summarised as follows:

Admittance documents D44-D46

Documents D44, D45 and D46 should not be admitted into the appeal procedure under Article 12(4) RPBA 2007 as these documents were not occasioned by the decision of the opposition division and could have been presented during the first instance proceedings.

Main request, clarity

Claim 1 of the main request clearly defined the tablet to comprise two specifically defined layers. The tablet could thus comprise further components. The definition of the amounts of the ingredients of the layers in %w/w in claim 1 evidently related to the amounts relative to the total weight of the two layers and not to the total weight of the final tablet.

Main request, inventive step

Claim 1 of the main request completely defined the layers of the tablet, which allowed to achieve bioequivalence with separate tablets of the individual active agents as evidenced by the bioavailability of the active agents from formulation 3 reported in the patent. The term "comprising" was frequently used in patents in the field of pharmacy and should not be interpreted to allow the inclusion of components that are incompatible with the teaching of the patent. In view of document D6 as closest prior art the problem to be solved was to be seen in the provision of a formulation containing the three active agents which is bioequivalent to specific separate reference products of the active agents. As solution to this problem the claimed subject-matter was not obvious from the prior art having regard to the influence of even small variations in the amounts of the excipients on the pharmacokinetics as shown in the patent for formulation 3 and formulation 4.

Auxiliary requests 1-11

Auxiliary requests 1-11 were intended to address different contingencies.

Claim 1 of auxiliary request 7 resolved in particular any issue related to the open terminology of claim 1 of the main request by specifically defining the tablet as consisting of the defined layers. Any issue of consistency regarding the coated tablet of claim 2 was resolved by formulation of claim 2 as an independent claim.

Claim 1 of auxiliary 11 resolved any issue regarding open terminology or inconsistency by specifically defining the tablet as consisting of the defined layers and optionally a film coating.

Auxiliary request 12

The claims of auxiliary request 12 were entitled to the priority of 19 November 2010 (US415600P). The claimed subject-matter was therefore not anticipated by the alleged public prior use of the COMPLERA / EVIPLERA product resulting from document D23.

The definition of the tablets as consisting of specific components in the claims of auxiliary request 12 further ensured that the defined tablets represented a solution to the problem of providing a tablet achieving bioequivalence with separate tablets of the individual active agents, which was not obvious from the prior art.

XI. The arguments of the appellant-opponent 1 in as far as relevant to the present decision can be summarised as follows:

Admittance documents D44-D46

The filing of documents D44, D45 and D46 was occasioned by the decision under appeal. These documents confirmed the strict concept of bioequivalence, in view of which the formulation of the problem to be solved in the decision under appeal was contested.

Main request, clarity

Claim 1 of the main request lacked clarity because the open definition of the tablet as comprising two layers was in contradiction to the definition of the amounts of the specific components of these layers to a total of 100% w/w.

Main request, inventive step

Document D6 already described a tablet comprising the combination of active agents defined in claim 1 of the main request. As solution to the problem of providing a stable alternative formulation for the three active agents, the preparation of a multi-layer tablet, keeping the rilpivirine HCl in association with a surfactant separate from the tenofovir disoproxil fumarate and the emtricitabine, was obvious in view of the known incompatibility of the tenofovir disoproxil fumarate with surfactants as described in document D3 and in view of the analogue bilayer tablet as described in document D33. The choice of the excipients was obvious in view of the known composition comprising rilpivirine HCl described in document D37 and the known composition comprising tenofovir disoproxil fumarate and emtricitabine described in document D43. The bioavailability data reported in the patent for the exemplified formulation 3 could not support an inventive step for the tablet as defined in claim 1 of the main request in view of the open definition of the tablet, which allowed additional components to be comprised in addition to the defined layers, and the influence of further components on the bioavailability, which was recognized in paragraph [0111] of the patent itself. The same analysis applied starting from document D1 as closest prior art, as this document also

described a tablet comprising the triple combination of active agents.

Auxiliary requests 1-11

The claims of auxiliary request 1 lacked clarity due to inconsistency, as independent claim 1 defined a tablet consisting of two specific layers, whereas the dependent claims 2 and 3 defined such a tablet as still comprising additional components.

Auxiliary requests 2, 4, 5, 6, 10 and 11 should not be admitted under Rule 80 EPC as these requests were aimed to overcome an objection of lack of clarity. Moreover these requests were not *prima facie* clearly allowable and should have been filed during the proceedings before the opposition division.

The claims of auxiliary requests 2, 4, 6-8 and 10-11 lacked an inventive step for similar reasons as the claims of the main request and the claims of auxiliary requests 3, 5 and 9 lacked clarity for similar reasons as the claims auxiliary request 1.

Auxiliary request 12

Claims 3 and 4 of auxiliary request 12 were not entitled to the priority of 19 November 2010 (US415600P). The public use of the COMPLERA / EVIPLERA product resulting from document D23 therefore represented prior art, in view of which the subject-matter of the claims of auxiliary request 12 lacked novelty.

The subject-matter of claims 1 and 2 of auxiliary request 12 did not involve an inventive step for

similar reasons as the main request. Taking account of the strict criteria for bioequivalence indicated in documents D44-D46 the bioavailability reported in the patent for the exemplified formulation 3 was not sufficient to establish bioequivalence of the claimed tablet with separate tablets comprising the single agents and did therefore not support an inventive step.

XII. The appellant-patent proprietors requested that the decision under appeal be set aside and that the patent be maintained on the basis of the main request or auxiliary requests 1-13, all filed with the grounds of appeal, but with renumbering of (previous) auxiliary request 13 as auxiliary request 11 and (previous) auxiliary requests 11 and 12 as auxiliary requests 12 and 13.

The appellant-patent proprietors further requested that documents D44-D46 submitted during the appeal procedure not be admitted.

XIII. The appellant-opponent 1 requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

The appellant-opponent 1 further requested that auxiliary requests 2, 4, 5, 6 and 10 as well as auxiliary requests 11 and 13 (both as renumbered) not be admitted.

XIV. The respondent-opponent 2 did not submit any requests or substantive observation during the appeal proceedings.

Reasons for the Decision

1. Admittance of documents D44-D46

The decision under appeal acknowledged bioequivalence of a combination tablet comprising rilpiverine HCl, emtricitabine, and tenofovir disoproxyl fumarate as defined in the patent with respect to separate tablets of the individual active agents on the basis of experimental results reported in the patent and document D6. This bioequivalence was an essential ground for opposition division's decision regarding the requirement of inventive step.

Documents D44-D46 were submitted by the appellant-opponent 1 with its grounds of appeal to support the argument that the evidence in the patent and document D6 was not sufficient to establish any bioequivalence and to contest in this respect the decision under appeal. Documents D44 and D45 describe criteria for establishing bioequivalence in the context of market authorisation applications for human medicinal products. Document D46 is from the same authors as document D6 and describes details of the bioequivalence study concerning a single tablet comprising emtricitabine, rilpiverine and tenofovir disoproxyl fumarate, which were not reported in document D6.

Taking account of the mentioned ground for the decision under appeal and the mentioned argument contesting this ground the Board considers the filing of D44-D46 to be part of a fair response to the decision under appeal and has therefore not exercised its discretion not to admit these documents into the proceedings.

2. Main request

2.1 Clarity

Amended claim 1 of the main request defines a tablet in line with the second embodiment of claim 15 of the patent as granted with additional definition of the amounts of the ingredients in terms of %w/w in line with paragraph [0063] of the patent.

Claim 1 of the main request specifically defines the tablet in an open manner as comprising two layers and thereby allows for further components to be present in the tablet, such as a third separating layer or a film coating as defined in dependent claims 2 and 3 of the main request. The introduced definition of the ingredients in terms of %w/w does not explicitly specify the basis for the percentage. However, the open definition of the tablet claim 1 evidently implies that the amounts of the ingredients defined in %w/w, which add up to a total of 100%, are to be calculated on the basis of the combined total weight of the two layers and not the weight of the entire tablet.

Contrary to the decision under appeal the Board therefore considers that the amendments in accordance with the main request comply with the requirement of clarity.

2.2 Inventive step

2.2.1 The patent relates to a single formulation comprising rilpiverine HCl, emtricitabine and tenofovir disoproxyl fumarate which is aimed at achieving chemical stability as well as equivalent plasma concentrations with

respect to separate reference products containing the single active agents (see paragraph [0007]).

Document D6 already describes a study investigating the bioequivalence of a tablet containing the triple combination of 25 mg rilpiverine, 200 mg emtricitabine and 300 mg tenofovir disoproxil fumarate with respect to separate formulations of the individual active agents. The tablet defined in claim 1 of the main request differs from this prior art in the defined structure separating the rilpiverine HCl from the emtricitabine together with the tenofovir disoproxil fumarate in two different layers and the definition of the excipients with their specific amounts.

Document D1, which also describes a triple combination of rilpiverine HCl, emtricitabine and tenofovir disoproxil fumarate in a single tablet (see page 20, table 2 and page 25, example 4), additionally differs from the subject-matter of claim 1 of the main request in the defined amount of rilpiverine HCl. The Board therefore agrees with the decision under appeal, that document D6 represents the closest prior art.

2.2.2 The Board observes that the patent presents experimental results indicating that a tablet consisting of two layers as defined in claim 1 of the main request and a specific film coat (see formulation 3 in paragraph [0105])

- shows stability of the active ingredients (see example 6, paragraph [0113]),
- allows for a specific pharmacokinetic profile in terms of AUC and Cmax for the defined three active ingredients in healthy adults under fed conditions, which resembles the profile resulting from

administration of separate reference dosage forms of these active ingredients indicative for bioequivalence (see example 5, paragraphs [0107] to [0112]) and

- preserves similar AUC values for rilpiverine HCl under fasted conditions (see example 8, paragraphs [0115]to [0118]).

The Board further notes that the patent also presents experimental results indicating that tablets with lower amounts of microcrystalline cellulose, lactose monohydrate and croscarmellose sodium in the rilpivirine HCl layer do not show the pharmacokinetic profile indicative for bioequivalence. (see formulation 4 in paragraph [0105] and the results discussed in paragraph [0111]).

2.2.3 The Board agrees with the appellant-opponent 1, that the subject-matter defined in claim 1 of the main request would be obvious to the skilled person, in as far as the problem solved is merely to be seen in the provision of a stable alternative co-formulation for the defined active agents. Having regard to the known incompatibility of tenofovir disoproxil fumarate with surfactants described in document D3 (see page 1-2 bridging paragraph) and in view of the analogue bilayer tablet described in document D33, in which efavirenz in association with a surfactant is formulated separately from tenofovir disoproxil fumarate and the emtricitabine (see D33, page 5/48 third full paragraph), the skilled person would be motivated to formulate rilpivirine HCl, which also requires a surfactant, in a layer separate from tenofovir disoproxil fumarate and the emtricitabine. Moreover, having regard to the known formulation of rilpivirine HCl as described in document D37 (see paragraph [0121])

and the known co-formulation of emtricitabine and tenofovir disoproxyl fumarate as described in document D43 (see Table 1 in paragraph [0121]), the skilled person would consider the choice of excipients as defined in claim 1 of the main request obvious as alternative.

2.2.4 According to the appellant-patent proprietors the problem underlying the subject-matter of claim 1 would not concern the provision of merely a stable alternative formulation, but should be seen in the provision of a formulation that is also bioequivalent with specific separate formulations of the active ingredients.

The Board observes in this context that claim 1 of the main request defines the tablet as *comprising* the two layers with the specific amounts of ingredients and thus allows for further components to be included in the tablet. This is confirmed by dependent claims 2 and 3 which define the tablet as further comprising a separating layer or a film coating. According to paragraph [0111] of the patent the difference in plasma concentrations of the active agents following administration of the bioequivalent formulation 3 and the non-bioequivalent formulation 4 reported in paragraph [0110] could have resulted from the influence of the higher amounts of diluents in the rilpivirine layer of formulation 3 on the interactions between rilpiverine and the other active agents. In view of the variation in pharmacokinetics from formulations 3 and 4, which only differ in the amounts of diluents in the rilpivirine layer, and the explanation for this variation postulated in the patent itself the Board is of the opinion that it is reasonable to assume that the pharmacokinetic profile from the tablet is likewise

influenced by the further inclusion of a third separating layer or the provision of a different coating or the inclusion or any further component. The Board therefore concludes that the subject-matter of claim 1 of the main request may not be presumed to generally represent within the entire scope of the claim a solution to the problem of providing a co-formulation of the defined active agents which shows the bioequivalence with respect to specific separate formulations of the active ingredients as reported in the patent for formulation 3.

In this context the Board is not convinced by the appellant-patent proprietors' arguments, that claim 1 of the main request completely defines the layers of the tablet essential for achieving the reported bioavailability of the active agents and that the term "comprising" as regularly used in the field of pharmacy should not be interpreted to allow inclusion of components that are incompatible with the teaching of the patent. As is evident from claims 2 and 3 of the main request, tablets including a separating layer or an alternative coating are embodiments covered by claim 1 of the main request and fully in line with the teaching of the patent. In view of the evidence on file as discussed above, such tablets including a separating layer or an alternative coating may not be presumed to generally represent a solution to the problem of providing a co-formulation of the defined active agents with the desired bioequivalence. In the Board's view the definition of the constitution of the tablets beyond the inclusion of the specific layers is thus essential for achieving the desired pharmacokinetic profile.

The problem underlying the subject-matter of claim 1 of the main request is therefore to be seen in the provision of a stable alternative co-formulation for the defined active agents. For the reasons explained in section 2.2.3 above the Board concludes that the subject-matter of claim 1 of the main request would be obvious to the skilled person as solution to such a problem in view of the prior art and therefore does not involve an inventive step. Accordingly, the main request is not allowed.

3. Auxiliary requests 1-11

3.1 Auxiliary request 1

Independent claim 1 of auxiliary requests 1 defines the tablet to consist of the two specifically defined layers and excludes thereby the inclusion of further components of the defined tablet. At the same time dependent claims 2 and 3 of auxiliary request define the tablet of claim 1 to further comprise a third separating layer or a film coating. Dependent claims 2 and 3 are therefore inconsistent with claim 1, which contrary to the requirements of Article 84 EPC gives rise to ambiguity as to what is intended to be covered by the claims. As this ambiguity is introduced by the amendments of the claims as granted auxiliary request 1 is not allowed.

3.2 Auxiliary requests 2-11

3.2.1 In auxiliary requests 2, 4, 6, 8 and 10 the independent claim 1 of the main request is maintained. These auxiliary request are therefore not allowed for the same reasons as explained in section 2.2 for the main request.

3.2.2 In claim 1 of each of auxiliary requests 3, 5 and 9 the tablet is defined as consisting of the two specific layers. At the same time dependent claim 2 of auxiliary request 3 defines such tablet to further comprise a film coating, whilst the dependent claims 2 in each of auxiliary requests 5 and 9 define such tablet to further comprise a separating third layer. Auxiliary requests 3, 5 and 9 thereby introduce the same ambiguity as identified in section 3.1 above with respect to auxiliary request 1. Auxiliary requests 3, 5 and 9 are therefore not allowed for the same reason as explained for auxiliary request 1.

3.2.3 Auxiliary request 7 defines in its claim 1 the tablet as consisting of the two specific layers and seeks to avoid the inconsistency occurring in auxiliary request 3 by formulating its claim 2 in an independent manner as directed to a film coated tablet comprising the tablet as defined in claim 1 and a film coating that covers a portion or all of the tablet. This formulation includes, however, the open terminology "comprising", in view of which the defined film coated tablet may include additional components that influence the pharmacokinetic profile of the active ingredients. Moreover, claim 2 of auxiliary request 7 does not define any restriction as to the composition of the coating and thus includes coatings that influence the bioavailability of the active agents. The Board is therefore of the opinion that the subject-matter of this claim may not be presumed to generally solve the the problem of providing a formulation with the desired pharmacokinetic profile equivalent to that of the specific separate formulations for the individual active agents. Accordingly, the subject-matter of claim 2 of auxiliary request 7 lacks an inventive step

for same reason as explained for claim 1 of the main request. Hence auxiliary request 7 is not allowed.

3.2.4 Auxiliary request 11 (previous auxiliary request 13) defines in its claim 1 the tablet as consisting of the two specific layers and optionally a film coating. In a similar manner as claim 2 of auxiliary request 7 this claim fails to define any restriction as to the composition of the coating and thus includes coatings that influence the bioavailability of the active agents as claim 2 of auxiliary request 7. The Board therefore concludes that this claim may also not be presumed to generally solve the problem of providing a formulation with the desired pharmacokinetic profile equivalent to that of the specific formulations with the single agents. Accordingly, claim 1 of auxiliary request 11 lacks an inventive step for same reason as explained for claim 1 of the main request. Hence auxiliary request 11 is not allowed.

In view of the Board's conclusions regarding the allowability of auxiliary requests 2-11 the request of appellant-opponent 1 not to admit auxiliary requests 2, 4, 5, 6, 10 and 11 remains without consequence.

4. Auxiliary requests 12 (previous auxiliary request 11)

4.1 The claims of auxiliary request 12 (as renumbered) correspond to the claims of auxiliary request 6 which was held allowable in the decision under appeal. Regarding this request the appellant-opponent 1 contested upon appeal only the findings of the opposition division with respect to the requirements of novelty and inventive step. The Board finds no grounds for reviewing any of the further findings in the decision under appeal regarding this request.

4.2 Novelty / Priority entitlement

Novelty of the defined subject-matter was contested by the appellant-opponent 1 in view of the alleged prior public use of the COMPLERA / EVIPLERA product as reported in document D23.

According to the decision under appeal no evidence of any public use of the COMPLERA / EVIPLERA product prior to the claimed priority date of 19 November 2010 resulted from the documents on file. This finding was not contested by the appellant-opponent 1.

The relevant priority document, US415600P, presents in its claim 23 a definition of a tablet in the same terms as claim 1 of auxiliary request 12. The priority document also discloses the composition of formulation 3 (see page 21), which corresponds to the coated tablet defined in claim 2 of auxiliary request 12. The priority document further indicates that the described tablets are for treatment of HIV infection and allow for achieving a similar level of rilpivirine AUC or Cmax in the patient when fasted or fed (see Summary of the invention on pages 3-4 and claims 26 and 27) in line with the definitions of claims 3 and 4 of the main request. The formal priority entitlement was not disputed during the appeal procedure. The Board is therefore of the opinion that the subject-matter of auxiliary request 12 is entitled to the priority of 19 November 2010.

Having regard to this effective date the Board concludes that the subject-matter defined in accordance with auxiliary request 12 meets the requirement of novelty.

4.3 Inventive step

4.3.1 Having regard to the experimental data presented in the patent as mentioned in section 2.2.2 above and in view of the limitation to tablets consisting of the quantitatively defined ingredients the Board is satisfied that claimed tablets provide the specific desired pharmacokinetic profile, which is equivalent to the profile from separate reference products of the individual agents.

In view of document D6 as closest prior art the problem solved may therefore be seen the provision of a co-formulation of the defined three active agents which is bioequivalent to specific separate reference products of the individual active agents. The Board agrees with the finding in the decision under appeal that the subject-matter defined in accordance with auxiliary request 12 was not obvious to the skilled person having regard to the influence of even small variations in the amounts of the excipients on the pharmacokinetics as confirmed in the patent for formulation 3 and formulation 4 (see paragraph [0110]).

4.3.2 With reference to the criteria for bioequivalence in the context of applications for market authorisations indicated in documents D44 and D45 the appellant-opponent 1 contested that the data in the patent allow for a conclusion as to bioequivalence of the claimed tablets. At the priority date no approved formulation for rilpiverine HCl was commercially available, that could have served as the reference formulation. Pharmacokinetic data would further vary considerably depending on the exact experimental conditions. The data in document D6 could not be used as a basis for

any meaningful comparison to establish bioequivalence, because the details of the experimental conditions, including the methods for determining the plasma levels and the definition of the study population, were not mentioned in document D6. Notably, such details were revealed in the post-published document D46.

The Board observes, however, that the experimental results presented in the patent still indicate the specific desired pharmacokinetic profile for the tested combination tablet, which resembles the profile from separate specific reference products of the individual agents. The data in the patent thereby substantiate that the identified problem is effectively solved. This relevance of the data in the context of the requirements for patentability is not affected by the applicable criteria for bioequivalence in the context of applications for market authorisation or by the argument that at the priority date no approved commercial product for rilpiverine HCl had been available.

4.4 Accordingly the Board confirms the conclusion in the decision under appeal that the patent as amended in accordance with auxiliary request 12 meets the requirements of the EPC.

Order

For these reasons it is decided that:

The appeals are dismissed

The Registrar: The Chairman:

S. Sánchez Chiquero A. Usuelli

Decision electronically authenticated