Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 12 April 2024

Case Number: T 1525/19 - 3.3.07

Application Number: 10703474.6

Publication Number: 2395984

IPC: A61P3/06, A61P3/08, A61P3/10, A61K31/522, A61K31/7048, A61K9/20, A61K9/36

Language of the proceedings: EN

Title of invention:

PHARMACEUTICAL COMPOSITION COMPRISING LINAGLIPTIN AND A SGLT2 INHIBITOR,AND USES THEREOF

Patent Proprietor:

Boehringer Ingelheim International GmbH

Opponents:

Generics (U.K.) Limited
STADA Arzneimittel AG
ZAKLADY FARMACEUTYCZNE POLPHARMA S.A.
Teva Pharmaceutical Industries Ltd.
Hexal AG

Headword:

Linagliptin-empagliflozin/BOEHRINGER

Relevant legal provisions:
EPC Art. 100(c), 87(1), 54(3), 56
RPBA Art. 12(4) (2007)
RPBA 2020 Art. 13(1)

Keyword:
Main request - added subject-matter (yes)
Auxiliary request 1 - admitted (yes) - priority (yes) - novelty (yes) - inventive step (yes)
Late-filed document - admitted (no)
Consideration of post-published evidence (yes)
Reopening the debate (no)
Staying the appeal proceedings (no)
Referring questions to the Enlarged Board of Appeal (no)

Decisions cited:
G 0001/22, G 0002/22, G 0002/21, G 0012/91, R 0010/08

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1525/19 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 12 April 2024

Appellant: (Opponent 1)	Generics (U.K.) Limited Building 4, Trident Place Mosquito Way Hatfield Herts AL10 9UL (GB)
Representative:	Ter Meer Steinmeister & Partner Patentanwälte mbB Nymphenburger Straße 4 80335 München (DE)
Appellant: (Opponent 2)	STADA Arzneimittel AG Stadastrasse 2-18 61118 Bad Vilbel (DE)
Representative:	Kernebeck, Thomas Kernebeck Patentanwalts GmbH Stiftstraße 2 60313 Frankfurt am Main (DE)
Appellant: (Opponent 3)	ZAKLADY FARMACEUTYCZNE POLPHARMA S.A. ul. Pelplinska 19 83-200 Starogard Gdanski (PL)
Representative:	Elkinton and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Party as of right: **(Opponent 4)**	Teva Pharmaceutical Industries Ltd. 124 Dvora HaNevi'a St. 6944020 Tel Aviv (IL)
Representative:	Kraus & Lederer PartGmbB Thomas-Wimmer-Ring 15 80539 München (DE)

Appellant: (Opponent 5)	Hexal AG Industriestraße 25 83607 Holzkirchen (DE)
Representative:	Elkington and Fife LLP Prospect House 8 Pembroke Road Sevenoaks, Kent TN13 1XR (GB)
Respondent: (Patent Proprietor)	Boehringer Ingelheim International GmbH Binger Straße 173 55216 Ingelheim (DE)
Representative:	Hoffmann Eitle Patent- und Rechtsanwälte PartmbB Arabellastraße 30 81925 München (DE)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 26 March 2019 rejecting the oppositions filed against European patent No. 2 395 984 pursuant to Article 101(2) EPC**

Composition of the Board:

Chairman	A. Usuelli
Members:	J. Molina de Alba
	M. Blasi

Summary of Facts and Submissions

I. The decision under appeal is the opposition division's decision rejecting the five oppositions filed against European patent No. 2 395 984.

II. The patent had been granted with 15 claims. Claims 1 and 15 as granted read as follows:

"*1. A solid pharmaceutical dosage form comprising linagliptin as a first active pharmaceutical ingredient in an amount of 5 mg and 1-chloro-4-(β-D-glucopyranos-1-yl)-2-[4-((S)-tetrahydrofuran-3-yloxy)-benzyl]-benzene as a second pharmaceutical ingredient in an amount of 10 mg or 25 mg and one or more excipients, wherein the term 'linagliptin' as employed herein refers to linagliptin and pharmaceutically acceptable salts thereof, including hydrates and solvates thereof, and crystalline forms thereof, and wherein the definition '1-chloro-4-(β-D-glucopyranos-1-yl)-2-[4-((S)-tetrahydrofuran-3-yloxy)-benzyl]-benzene' also comprises its hydrates, solvates and polymorphic forms thereof.*"

"*15. The pharmaceutical dosage form according to one or more of the previous claims characterized in that it is a one layer tablet in which the two active pharmaceutical ingredients are present in the one layer.*"

In this decision, the second active ingredient is also referred to by its common name, empagliflozin.

III. The following documents are referred to in the present decision:

D1 WO 2009/022007 A1

D2 US 2007/0281940 A1

D3 WO 2005/092877 A1

D4 WO 2004/018468 A2

D8 WO 2007/128761 A2

D17 Y. Wang, Drugs of the Future, 2008, 33(6), 473-7

D20 CA 2651019 A1

D23 S. Hüttner et al., J Clin Pharmacol, 2008, 48, 1171-8

D24 L. Thomas et al., JPET, 2008, 325(1), 175-82

D26 WO 2008/055940 A2

D33 A.E. Weber, J. Med. Chem., 2004, 47, 4135-41

D43 A. Lewin et al., Diabetes Care, 2015, 38, 394-402

D44 R.A. DeFronzo et al., Diabetes Care, 2015, 38, 384-93

D45 F. Schernthaner et al., Diabetes, Obesity and Metabolism, 2015, 17, 613-5

D56 G. Charpentier, Diabetes Metab Res Rev, 2002, 18, S70-S76

D57 G. Derosa et al., Vascular Health and Risk Management, 2007, 3(5), 665-71

D58 J.E. Gerich, Clinical Therapeutics, 2001, 23(5), 646-59

D62 Experimental report entitled "Effect of Linagliptin and an SGLT2 inhibitor and its combination on active GLP-1 in diabetic ZDF rats"

D63 L.L. Baggio et al., Gastroenterology, 2007, 132(6), 2131-57

D64 Experimental report entitled "Comparison of treatments with empagliflozin"

D67 E. Ferrannini et al., J Clin Invest., 2014, 124(2), 499-508

D68 DrugBank entries for "Linagliptin", "Sitagliptin" and "Vildagliptin"

D73 J. Rosenstock et al., Diabetes Care, 2015, 38, 376-83

D74 L. Thomas et al., JPET, 2009, 328(2), 556-63

D79 Clinical study synopsis for public disclosure, Trial No. 1275.1/U13-2755-01, Boehringer Ingelheim

IV. In the decision under appeal, the opposition division concluded in relation to the patent as granted that:

- the claimed subject-matter did not extend beyond the content of the application as filed and was sufficiently disclosed,
- D1 was prior art under Article 54(3) EPC because the claimed subject-matter enjoyed the priority date of 13 February 2009,
- the subject-matter of claim 1 was novel over D1,
- D2 and D3 could be considered to be the closest prior art; the objective technical problem was the provision of a combination medication for achieving advantageous effects on HbA1c and GLP-1 levels; the solution proposed in claim 1 was not obvious.

V. Opponents 1, 2, 3 and 5 (appellants 1, 2, 3 and 5) each filed an appeal against the decision.

Opponent 4 (party as of right) filed an appeal that it subsequently withdrew with a letter dated 10 October 2023.

The patent proprietor is respondent in these appeal proceedings.

VI. In their statements of grounds of appeal, the appellants requested that the opposition division's decision be set aside and that the patent be revoked in its entirety.

VII. With its reply to the statements of grounds of appeal, the respondent requested that the appeals be dismissed (main request). In addition, it filed nine sets of claims as auxiliary requests 1 to 9.

The claims of auxiliary request 1 are identical to those of the patent as granted, with the exception that claim 15 has been deleted.

VIII. With a letter filed in response to the respondent's reply to the statements of grounds of appeal, appellant 5 filed document D79.

IX. The board scheduled oral proceedings, in line with the parties' requests, and set out its preliminary opinion on the case.

X. Oral proceedings were held before the board on 1 September 2023, with all parties present. At the end of the oral proceedings, the board announced the following conclusions on the issues discussed and closed the debate on those issues:

- the added subject-matter objection raised by appellant 1 in its statement of grounds of appeal (point 3) was not admitted into the proceedings,
- claim 15 as granted added subject-matter,

- auxiliary request 1 was admitted into the proceedings,
- the subject-matter of auxiliary request 1 was novel over D1,
- D79 was not admitted into the proceedings,
- the subject-matter of auxiliary request 1 was inventive starting from either D2 or D3 as the closest prior art,
- the inventive step objection starting from linagliptin monotherapy as the closest prior art was not admitted.

Since the issue of whether D1 could be considered for the assessment of inventive step depended on the decision of the Enlarged Board of Appeal in referral cases G 1/22 and G 2/22, which were pending at that time, the oral proceedings were adjourned.

XI. In a communication dated 16 November 2023, the board informed the parties that a decision in cases G 1/22 and G 2/22 had been handed down. In light of this decision, the priority date of 13 February 2009 seemed to be validly claimed, with the consequence that D1 could not be considered for the assessment of inventive step. Therefore, the board could take a decision on the case without holding further oral proceedings. The board gave the parties two months to comment on the issues on which the debate had not yet been closed.

XII. None of the parties contested the board's conclusions that the priority date of 13 February 2009 was validly claimed and that D1 therefore could not be considered for the assessment of inventive step. However, appellants 1 and 5 requested that the debate on inventive step be reopened because, in the meantime, Board 3.3.04 had taken a decision in a related appeal

case, T 314/20, which allegedly contradicted the conclusion of the present board at the end of the oral proceedings on 1 September 2023. Appellant 1 also requested that the appeal proceedings be stayed until the reasons of T 314/20 are issued in writing. In the alternative, appellant 1 requested that questions on the interpretation of decision G 2/21 be referred to the Enlarged Board of Appeal.

XIII. The board summoned the parties to oral proceedings to hear them on the issues of whether the debate on inventive step should be reopened, whether the proceedings should be stayed, and whether questions should be referred to the Enlarged Board of Appeal.

XIV. In preparation for the oral proceedings, appellants 1 and 5 and the respondent filed further submissions. Appellant 3 advised the board that it would not be attending the oral proceedings.

XV. Oral proceedings were held before the board on 12 April 2024 in the absence of appellants 2 and 3 and the party as of right. At the end of the oral proceedings, the board announced its decision.

XVI. The appellants' arguments relevant to the present decision can be summarised as follows.

Added subject-matter - main request

The subject-matter of claim 15 as granted resulted from a double selection to the extent that it depended on claims 2 and 3 as granted: first, the selection of one of the alternatives on page 38, lines 2 to 15 (a one layer tablet), and second, the selection of two of the

alternatives in the table on pages 39 and 40 (5 mg linagliptin and 10 or 25 mg empagliflozin).

Admittance of auxiliary request 1

The claims of auxiliary request 1 were the claims as granted, with the exception that claim 15 had been deleted. The deletion of claim 15 was a response to an added subject-matter objection raised by appellant 5 in its notice of opposition. Therefore, auxiliary request 1 should have been filed in the opposition proceedings and should not be admitted in appeal proceedings.

Novelty - auxiliary request 1

D1 disclosed all of the features in claim 1 in combination. Compound (9) was empagliflozin and compound (A) was linagliptin. Entry 97 in Table 1 disclosed the combination of empagliflozin with linagliptin. This was one of the five most preferred combinations, all of which contained empagliflozin (page 33, line 4). D1 also disclosed a list of six preferred amounts of empagliflozin, including 10 and 25 mg (page 39, lines 29 to 31). The amount of linagliptin was preferably 1, 2.5 or 5 mg (page 40, lines 15 and 16). Shortening the list of six preferred amounts of empagliflozin to 10 and 25 mg was not a selection because there was no singling-out of one element. The only selection was the choice of 5 mg linagliptin. In any case, there was no real selection from two lists because the total number of combinations was very limited. Therefore, the combination of 5 mg linagliptin with 10 or 25 mg empagliflozin was disclosed in D1. As to the feature of the solid dosage form, this was the preferred form in D1 and therefore no selection was needed here either.

Inventive step - auxiliary request 1

D2 was the closest prior art. Example 15 taught that the combination of a DPP-IV inhibitor with a SGLT2 inhibitor led to a significantly greater reduction in glucose levels than either the DPP-IV inhibitor alone or the SGLT2 inhibitor alone. The dosage form of claim 1 was encompassed by Example 15 of D2. The distinguishing features of claim 1 of auxiliary request 1 over D2 were that claim 1 specified the DPP-IV inhibitor and the SGLT2 inhibitor as well as their corresponding amounts.

Yet these distinguishing features were not associated with any technical effect. The combinations in Example 15 reduced glucose levels to a greater extent than either monotherapy. This teaching was credible because it was based on the common general knowledge that the combination of two active compounds acting by different mechanisms could be expected to produce an effect greater than the effect of either monotherapy. This was also the effect observed in Example I of the patent.

The respondent had not shown that the active compound combinations in claim 1 were better than other combinations encompassed by Example 15 of D2. Post-published documents D43, D44, D45, D62 and D64 did not allow the consideration of any additional technical effect. Firstly, the clinical tests in D43, D44 and D45 showed that the combination of linagliptin with empagliflozin produced a subadditive effect on HbA1c. In fact, they showed that the combination of 5 mg linagliptin with 25 mg empagliflozin was no better than empagliflozin alone. Secondly, the data in D62 and D64

could not be taken into account, in accordance with decision G 2/21, because they showed a technical effect that was not derivable from the application as filed. In the application, the effect on GLP-1 was attributed to linagliptin alone. An effect of SGLT2 inhibitors on GLP-1 was observed for the first time only years after the filing date in a clinical study reported by the respondent in D67. In D67, the respondent considered it surprising that empagliflozin had an effect on GLP-1 levels. In addition, the tests in D62 and D64 had been carried out on animals and could not be considered to be more relevant than the clinical tests reported in D43, D44 and D45, which showed that the combination in claim 1 did not provide any improvement in controlling glycaemia in humans. Furthermore, the doses administered in D62 and D64 were much higher than those defined in claim 1. Moreover, D64 failed to show a superior effect for the combination containing linagliptin compared with combinations containing other DPP-IV inhibitors according to D2, and most of the data therein were not statistically significant in any case.

Therefore, the objective technical problem was to provide an alternative composition for treating diabetes.

The solution proposed in claim 1 was obvious. Combining antidiabetic agents acting by different mechanisms was a common strategy for treating type-2 diabetes, as shown by D56, D57 and D58. Furthermore, linagliptin was a preferred DPP-IV inhibitor in D2 and empagliflozin was encompassed by the generic formula of SGLT2 inhibitors disclosed at the bottom of page 7, left-hand column, of that document. D3 also suggested the combination of SGLT2 inhibitors with DPP-IV inhibitors

(page 44, line 3) and disclosed empagliflozin as being a preferred SGLT2 inhibitor (page 26, compound 3).

Even if the data in D62 and D64 were taken into consideration, the technical effect they showed was obvious. D33 stated that DPP-IV inhibitors were particularly suitable for combination therapy with other diabetic treatments, and that combinations thereof could result in a synergistic effect. D24 and D74 taught that linagliptin was advantageous over other DPP-IV inhibitors. Furthermore, the advantageous effect of linagliptin over other DPP-IV inhibitors could be expected on the basis of its longer half-life, known from D68, or its longer-lasting effect, known from D73. The choice of empagliflozin as a combination partner was obvious from D26, because it was a preferred SGLT2 inhibitor (compound 3) to be orally administered at a daily dose of 10 to 50 mg (Example III).

D3 could also be taken as the closest prior art. It disclosed the preparation of empagliflozin, its use for treating diabetes, and its combination with other antidiabetic agents, including DPP-IV inhibitors.

The subject-matter of claim 1 differed from D3 in that linagliptin was combined with empagliflozin in given amounts. However, this difference did not produce any technical effect. The objective technical problem was still to provide an alternative composition for treating diabetes.

The solid dosage form of claim 1 was obvious from a combination of D3 with D2, D4, D17 or D24, which disclosed the superiority of linagliptin over other DPP-IV inhibitors.

Reopening the debate - staying the appeal proceedings - referring questions to the Enlarged Board of Appeal

The debate on the consideration of post-published evidence under decision G 2/21 should be reopened to avoid a possible contradiction with the decision in related appeal case T 314/20.

According to appellant 1, the appeal proceedings should be stayed until the written reasoned decision in appeal case T 314/20 is issued, because the reasons in that appeal could render it necessary to reopen the debate in the present appeal proceedings. A stay of the proceedings was also justified under Article 20(1) RPBA 2020. If the proceedings were not stayed and the debate was not reopened, then questions on the interpretation of decision G 2/21 should be referred to the Enlarged Board of Appeal.

Appellant 5 argued that the board's decision to consider post-published evidence under decision G 2/21 was based on an argument raised for the first time by the board during the oral proceedings of 1 September 2023. Appellant 5 had reacted to this argument with legal considerations that were rejected. Subsequently, during the oral proceedings in appeal case T 314/20, Board 3.3.04 had heard the appellants on the same issue, but this time including technical arguments. Since Board 3.3.04, having heard the case in full, had concluded that decision G 2/21 did not allow the consideration of post-published evidence, the present board should reopen the debate to also hear the technical arguments and avoid contradictory decisions.

XVII. The respondent's arguments relevant to the present decision can be summarised as follows.

Added subject-matter - main request

A one-layer tablet containing 5 mg linagliptin and 10 or 25 mg empagliflozin was disclosed in the following passages of the application as filed:

- page 7, lines 3 and 4,
- page 38, line 2,
- table on pages 39 and 40,
- page 44, line 27,
- example formulations on page 45, and
- Examples 1 to 5 and 8.

These passages taught that a one-layer tablet was the most preferred dosage form. Therefore, this could be combined with embodiments E2.15 and E.19 on page 40.

Admittance of auxiliary request 1

The deletion of claim 15 was a response to the added subject-matter objection raised by appellant 5 in its statement of grounds of appeal. Although appellant 5 had raised this objection in its notice of opposition, the respondent had replied to it and the issue was not discussed any further in the opposition proceedings. The opposition division gave a positive preliminary opinion on claim 15 and the issue was not discussed at oral proceedings. Therefore, there was no need to file auxiliary request 1 in the opposition proceedings. In addition, the deletion of claim 15 did not change the respondent's case and it was not detrimental to

procedural economy. Therefore, the request should be admitted.

Novelty - auxiliary request 1

The criterion to be applied for assessing whether D1 disclosed the subject-matter of claim 1 was the gold standard. D1 disclosed the combination of empagliflozin and linagliptin as one among a number of preferred combinations. However, it did not disclose the amounts specified in claim 1 for that particular formulation, nor that they should be provided in a solid dosage form. To arrive at the subject-matter of claim 1, it was necessary to select from three lists: the amount of empagliflozin (page 39, line 29); the amount of linagliptin (page 40, line 16); and the dosage form (page 44, line 16). These selections were not made from converging lists but from lists of mutually exclusive elements. Appellant 3's argument on the length of the lists and the number of total combinations was flawed. Appellant 5 was also wrong to consider that limiting the list of empagliflozin amounts to 10 and 25 mg was not a selection. The passages on page 39, line 29 and page 40, line 16, disclosed generic preferred amounts, not specific amounts for the combination of empagliflozin and linagliptin. The only passage explicitly disclosing amounts for that combination was page 41, line 25, which specified 5 to 50 mg empagliflozin and 0.5 to 10 mg linagliptin.

Inventive step - auxiliary request 1

The disclosure of D2 was speculative. It suggested the use of a group of selected DPP-IV inhibitors, including linagliptin, for treating diabetes. According to paragraph [0044], the selected DPP-IV inhibitors had

advantages over other DPP-IV inhibitors, but no evidence of this was provided. Based on the idea that the combination of active compounds acting by different mechanisms may provide an effect greater than monotherapy, D2 proposed the combination of DPP-IV inhibitors with other antidiabetic compounds, including SGLT2 inhibitors. Empagliflozin was encompassed, though not singled out, by the generic formula of the proposed SGLT2 inhibitors. Example 15 merely speculated that a generic combination of a DPP-IV inhibitor with a SGLT2 inhibitor in generic amounts could reduce glucose and HbA1c levels to a greater extent than either monotherapy. The example did not disclose specific combinations or experimental results.

The subject-matter of claim 1 differed from the combination in Example 15 of D2 in the choice of the active compounds and their respective amounts. These differences resulted in an unexpected advantage, as evidenced by Example I of the patent: the combination of linagliptin with empagliflozin reduced glycaemia to an extent not only greater than the effect of either component but also greater than the addition of their effects. This unexpected reduction in glycaemia was due to an overadditive increase in GLP-1 levels, as confirmed by D62 and D64. It also resulted in a reduction in HbA1c levels beyond the levels reached by either monotherapy, as confirmed by D43, D44 and D45. Furthermore, high GLP-1 levels promoted beta-cell regeneration and neogenesis (application and D63).

Contrary to the appellants' contentions, the data in D43, D44, D45, D62 and D64 were relevant. The standard before the EPO was not that of regulatory authorities but a balance of probabilities. In addition, the technical effect shown for the animal model in D62 and

D64 was credible for humans receiving the doses of linagliptin and empagliflozin usually administered when treating glycaemic disorders (e.g. D17, D23 and D26).

The principles of decision G 2/21 allowed to take into account the effect shown in D62 and D64. Claim 1 was directed to a specific combination of a DPP-IV inhibitor and a SGLT2 inhibitor that reduced glycaemia in an overadditive way, as demonstrated in Example I of the application. The application taught that DPP-IV inhibitors reduced glycaemia by increasing GLP-1 levels. Therefore, combinations thereof were expected to also increase GLP-1 levels. The extent of this increase, including a potential contribution by the SGLT2 inhibitor, was not a separate technical effect. It was only relevant for comparison with the closest prior art. Therefore, the technical effect in D62 and D64 was encompassed and embodied by the application as filed.

The objective technical problem was to provide a combination medication for achieving advantageous effects on HbA1c and GLP-1 levels.

D2 suggested the combination of DPP-IV inhibitors with many different drugs, SGLT2 inhibitors being just one possible option. There was no suggestion to combine linagliptin with empagliflozin, let alone to achieve an unexpected effect on HbA1c and GLP-1 levels. Similarly, D3 disclosed many possible combination partners for SGLT2 inhibitors. A DPP-IV inhibitor was one option among many and linagliptin was not cited at all.

D33 did not mention either linagliptin or empagliflozin. D24 and D74 did not refer to

empagliflozin, either. D26 did not suggest combining DPP-IV inhibitors with SGLT2 inhibitors.

Consequently, there was no suggestion in the cited documents that the combination of linagliptin with empagliflozin could produce unexpected HbA1c and GLP-1 levels.

Starting from D3, the subject-matter of claim 1 was not obvious, either. As when starting from D2, the appellants' arguments missed the point that the objective technical problem was not to provide an alternative composition but a composition with advantageous effects on HbA1c and GLP-1 levels.

Reopening the debate - staying the appeal proceedings - referring questions to the Enlarged Board of Appeal

The debate on the consideration of post-published evidence under decision G 2/21 should not be reopened. Once the debate has been closed, further submissions by the parties should be disregarded (R 10/08, referring to G 12/91). There were no exceptional circumstances to reopen the debate because the parties had already been heard on the contentious issue. There was no risk of contradictory decisions because the facts and arguments on which appeal T 314/20 was based were different from those underlying the case at hand. For the same reasons, staying the proceedings or referring questions to the Enlarged Board of Appeal was not justified either. In addition, the technical arguments raised by appellant 5 were submitted late and should not be admitted.

XVIII. The appellants' final requests were as follows:

- Appellants 1, 2, 3 and 5 requested that the decision under appeal be set aside and that the patent be revoked in its entirety.

- Appellant 1 also requested that the appeal proceedings be stayed until the written reasoned decision in appeal case T 314/20 be issued, and that the debate on inventive step be reopened in a new oral proceedings. As an auxiliary measure, appellant 1 requested that the questions on the interpretation of decision G 2/21 as filed by the respondent during the oral proceedings in appeal case T 314/20 be referred to the Enlarged Board of Appeal.

- Appellant 5 also requested that auxiliary requests 1 to 9 not be admitted into the appeal proceedings and that D79 be admitted. In addition, appellant 5 requested that the debate on inventive step be reopened.

XIX. The respondent's final requests were as follows:

- The respondent requested that the appeals be dismissed, or, alternatively, that the patent be maintained in amended form on the basis of one of the sets of claims filed as auxiliary requests 1 to 9 with the reply to the statements of grounds of appeal.

- The respondent also requested that documents D3a, D73a, D76, D77, D77a, D78a and D79 not be admitted into the appeal proceedings.

- In addition, the respondent requested that the debate not be reopened and that questions not be referred to the Enlarged Board of Appeal.

XX. The party as of right did not make any requests after withdrawing its appeal.

Reasons for the Decision

1. Admittance of the added subject-matter objection against claim 1 as granted (Article 12(4) RPBA2007)

In the decision under appeal, the opposition division concluded that claim 1 as granted did not add subject-matter. In its statement of grounds of appeal, appellant 1 submitted that it maintained the arguments it had made in its notice of opposition regarding the claims as granted adding subject-matter. Those arguments were directed against claim 1.

In its communication in preparation for the oral proceedings of 1 September 2023, the board noted that the basis for claim 1 as granted in the application as filed as discussed in appellant 1's notice of opposition was different from the basis discussed in the decision under appeal. However, appellant 1 had not explained in which respect the decision under appeal was flawed. Therefore, the board was minded not to admit the added subject-matter objection under Article 12(4) RPBA 2007 because the requirements of Article 12(2) RPBA 2007 were not met.

Appellant 1 did not reply to the board's preliminary opinion, nor did it wish to comment on this point at the oral proceedings of 1 September 2023. Therefore, the board did not admit the added subject-matter objection against claim 1 as granted under Article 12(4) RPBA 2007.

2. Amendments (Article 100(c) EPC) - claim 15 as granted

2.1 Appellant 5 argued that claim 15 as granted adds subject-matter to the extent that it depends on claims 2 and 3 as granted. The board agrees.

2.2 Claim 2 requires that linagliptin and empagliflozin be present in the pharmaceutical dosage form in amounts of 5 and 10 mg, respectively. Similarly, claim 3 requires that linagliptin and empagliflozin be present in amounts of 5 and 25 mg, respectively.

To the extent that claim 15 depends on claims 2 and 3, it is directed to a one-layer tablet in which linagliptin and empagliflozin are present in the single layer of the tablet in amounts of 5 mg and 10 or 25 mg, respectively.

2.3 The main basis for this claim in the application as filed is the passage on page 38, lines 2 to 4, and embodiments E2.15 and E2.19 in the table bridging pages 39 and 40.

The passage on page 38, lines 2 to 4, discloses a one-layer tablet containing linagliptin and empagliflozin in this one layer. However, this is merely one of several alternatives disclosed in the same paragraph with the same level of preference. Other alternatives include a two-layer tablet containing one active agent

in each of the layers, a film-coated tablet with one active ingredient in the core and the other in the coating film, etc.

Embodiments E2.15 and E.19 in the table bridging pages 39 and 40 disclose the combination of 5 mg linagliptin with 10 and 25 mg empagliflozin, respectively. These are two among 21 combinations of linagliptin and empagliflozin disclosed in the table.

There is no direct and unambiguous link between the option of a one-layer tablet as disclosed on page 38 and embodiments E2.15 and E.19. Therefore, the combination of features in claim 15 as granted adds subject-matter.

2.4 The respondent argued that a one-layer tablet was the most preferred dosage form in the application as filed and could therefore be combined with embodiments E2.15 and E.19. It referred to page 7, lines 3 and 4, page 44, line 27, the example formulations on page 45, and Examples 1 to 5 and 8.

The passage on page 7, lines 3 and 4, refers to "*tablets, such as one-layer tablets or two-layer tablets*".

The passage on page 44, line 27, discloses the preparation of one-layer tablets. This passage is in a section of the application as filed disclosing the preparation of several dosage forms according to the invention, including e.g. two-layer tablets (page 44, line 35).

The passage on page 45, line 6, refers to a one-layer tablet as an example of formulation according to the

invention, but it also refers to two-layer tablets in line 34. Subsequently, on page 46, lines 14 to 18, it refers to a film-coated tablet as another formulation example.

Examples 1 to 5 and 8 disclose different methods for preparing one-layer tablets, but Examples 6 and 7 disclose two-layer tablets. In addition, each example contains five embodiments with different amounts of linagliptin and empagliflozin. Only two of the embodiments in each example contain 5 mg linagliptin and 10 or 25 mg empagliflozin.

Consequently, none of the additional passages cited by the respondent teaches that a one-layer tablet is more preferred than other dosage forms, such as a two-layer tablet. A direct link between a one-layer tablet and the amount of active ingredients in claims 2 and 3 as granted is not directly and unambiguously disclosed.

2.5 Therefore, the ground for opposition under Article 100(c) EPC prejudices the maintenance of the patent as granted.

3. Admittance of auxiliary request 1 (Article 12(4) RPBA 2007)

3.1 Auxiliary request 1 was filed by the respondent with its reply to the statements of grounds of appeal, dated 2 August 2019. Therefore, the relevant provision for its admittance is Article 12(4) RPBA 2007 (see also Article 25(2) RPBA 2020).

3.2 The claims of auxiliary request 1 are identical to those of the patent as granted, with the exception that claim 15 has been deleted. The deletion of claim 15 was

a response to the added subject-matter objection raised by appellant 5 in its statement of grounds of appeal. This objection had first been raised in appellant 5's notice of opposition.

In its reply to the notices of opposition, the respondent had contested the added subject-matter objection raised against claim 15 as granted. In its preliminary opinion, the opposition division took the view that claim 15 did not add subject-matter. The objection was not discussed any further in the written opposition proceedings and the appellants made no further comments on it at the oral proceedings before the opposition division. In its decision, the opposition division confirmed its preliminary opinion that claim 15 as granted did not add subject-matter.

3.3 Considering the sequence of events above and the complex nature of the case, the board sees no reason why the respondent should have filed auxiliary request 1 during the opposition proceedings. The five opponents had raised a large number of objections against various claims and relating to all grounds for opposition under Article 100(a), (b) and (c) EPC. The objection dealt with by auxiliary request 1 was directed to a dependent claim. The objection had not been prosecuted by appellant 5 beyond its notice of opposition even if, subsequently, it had been refuted by the respondent with counter-arguments and the opposition division had agreed with the respondent on that point. Under such circumstances, the respondent could not be expected to file auxiliary request 1 in the opposition proceedings. Furthermore, the deletion of claim 15 in auxiliary request 1 overcomes the objection in a straightforward manner without

introducing further issues and without substantially changing the factual and legal framework of the case.

Therefore, the board admitted auxiliary request 1 under Article 12(4) RPBA 2007.

4. Priority (Article 87(1) EPC) - auxiliary request 1

4.1 Appellants 2 and 5 raised inventive-step objections based on D1, a PCT-application published between the priority date and filing date of the patent. In order to establish whether D1 belonged to the prior art under Article 54(2) EPC and could therefore be considered for the assessment of inventive step, it had to be decided whether the priority date was validly claimed.

4.2 It was not contested that the priority application discloses the same invention, within the meaning of Article 87(1) EPC, as claimed in auxiliary request 1. The only issue at stake was whether the applicant, Boehringer Ingelheim International GmbH, was entitled to claim the priority of US patent application 61/152,306, filed by Mr Eisenreich on 13 February 2009.

4.3 The Enlarged Board of Appeal held in its decision on consolidated cases G 1/22 and G 2/22 that:

(a) The European Patent Office is competent to assess whether a party is entitled to claim priority under Article 87(1) EPC.

There is a rebuttable presumption under the autonomous law of the EPC that the applicant claiming priority in accordance with Article 88(1) EPC and the corresponding

Implementing Regulations is entitled to claim priority.

(b) The rebuttable presumption also applies in situations where the European patent application derives from a PCT application and/or where the priority applicant(s) are not identical with the subsequent applicant(s).

In a situation where a PCT application is jointly filed by parties A and B, (i) designating party A for one or more designated States and party B for one or more other designated States, and (ii) claiming priority from an earlier patent application designating party A as the applicant, the joint filing implies an agreement between parties A and B allowing party B to rely on the priority, unless there are substantial factual indications to the contrary.

4.4 Thus, in accordance with decision G 1/22 and G 2/22, the board is competent to assess whether the applicant was entitled to claim priority under Article 87(1) EPC. In this context, there is a rebuttable presumption that the applicant was entitled to claim priority in situations including the one at hand, in which the European patent application derives from a PCT application and the priority applicant differs from the subsequent applicant.

The opponents have not rebutted the presumption that the applicant, Boehringer Ingelheim International GmbH, was entitled to claim the priority of US patent application 61/152306, filed by Mr Eisenreich. Therefore, the board concludes that Boehringer Ingelheim International GmbH was entitled to claim that

priority, with the consequence that the subject-matter claimed in auxiliary request 1 enjoys the priority date of 13 February 2009. This means that D1 does not belong to the prior art under Article 54(2) EPC and cannot be taken into consideration for the assessment of inventive step.

This had already been outlined by the board in its communication dated 16 November 2023, and was not contested by the parties.

5. Novelty (Article 54(3) EPC) - auxiliary request 1

5.1 It follows from the above finding on priority that D1 is prior art under Article 54(3) EPC. According to appellants 1, 3 and 5, D1 anticipates the solid dosage form of claim 1. The board disagrees.

5.2 D1 is directed to the combination of a glucopyranosyl-substituted benzene derivative of Formula (I) with a DPP-IV inhibitor. The compound of Formula (I) designated as "compound (9)" is empagliflozin, and the DPP-IV inhibitor designated as "compound (A)" is linagliptin (page 64, lines 21 and 22, and page 40, lines 13 to 15). In general, the preferred amounts of empagliflozin are 5, 10, 15, 20, 25 and 50 mg, and the preferred amounts of linagliptin are 1, 2.5 and 5 mg (page 39, lines 29 to 31, and page 40, lines 15 and 16).

Table 1, spanning from page 29 to 33, discloses 176 combinations of a glucopyranosyl-substituted benzene derivative with a DPP-IV inhibitor. The combinations of entries 97, 165, 166, 167 and 168 are the most preferred ones (page 33, line 4). They correspond to the combination of empagliflozin with linagliptin,

sitagliptin, vildagliptin, saxagliptin and alogliptin. The passage on page 41, lines 25 to 28, discloses the preferred amounts of empagliflozin and linagliptin when they are combined with each other. These are 5 to 50 mg empaglifozin and 0.5 to 10 mg linagliptin. Equivalent disclosures can be found on page 41, line 30 to page 42, line 8, for combinations of empagliflozin with sitagliptin, vildagliptin, alogliptin and saxagliptin. The amount of empagliflozin is always 5 to 50 mg.

5.3 The appellants argued that the list of preferred empagliflozin amounts was short and that its limitation to only two options, 10 and 25 mg, did not constitute a selection. Therefore, the only selection required was that the amount of linagliptin was 5 mg. The appellants also argued that the lists of empagliflozin and linagliptin amounts were short and contained a limited number of combinations. Therefore, the features in claim 1 resulted from a single selection within that limited number of combinations.

5.4 As pointed out by the respondent, the correct principle for assessing whether D1 discloses the subject-matter of claim 1 is the so-called "gold standard", i.e. what the skilled person would derive directly and unambiguously, using common general knowledge, and seen objectively from the prior-art document as a whole. This does not exclude the principle of selection from different lists as a tool, but the prevailing principle is whether the prior-art document discloses a direct and unambiguous link between the features in claim 1.

D1 teaches that the preferred amounts of empagliflozin are 5, 10, 15, 20, 25 and 50 mg, while those of linagliptin are 1, 2.5 and 5 mg. Nevertheless, these amounts are generally applicable and are not linked to

the particular combination of empagliflozin and linagliptin.

Table 1 discloses 176 combinations. Some of them contain empagliflozin but not linagliptin and vice versa. The combination of empagliflozin with linagliptin is one of the five most preferred combinations. The only passage in D1 which discloses the amounts of empagliflozin and linagliptin when they are combined with each other is on page 41, line 25: empagliflozin is present at 5 to 50 mg and linagliptin at 0.5 to 10 mg. Subsequently, equivalent passages disclose the amounts for the other most preferred combinations.

Therefore, the board cannot see in D1 a direct and unambiguous disclosure that when empagliflozin is combined with linagliptin, empagliflozin should be present at 10 or 25 mg, and that when linagliptin is combined with empagliflozin, linagliptin should be present at 5 mg. For this reason alone, the subject-matter of claim 1 is not anticipated by D1. Considerations on the presence of a further link to a solid dosage form are not required.

5.5 Therefore, the solid dosage form of claim 1 is novel over D1. As claim 1 is the only independent claim, auxiliary request 1 meets the requirements of Article 54(3) EPC.

6. *Admittance of document D79 (Article 13(1) RPBA 2020)*

D79 was filed by appellant 5 with its letter dated 19 April 2021, i.e. at a stage when the respondent had already replied to the appeals, to cast doubt on the relevance of the data in post-published documents D43,

D62 and D64. The relevance of those data had been extensively discussed between the parties throughout the opposition and at the beginning of the appeal proceedings. No new element was raised justifying the filing of D79 at such a late stage of the appeal proceedings. Appellant 5 did not give any reason for the late filing of D79 and made no comments in this respect at the oral proceedings before the board. Therefore, the board decided not to admit D79 under Article 13(1) RPBA 2020 (see also Article 25(1) RPBA 2020).

7. Inventive step (Article 56 EPC) - auxiliary request 1

7.1 Claim 1 is directed to a solid pharmaceutical dosage form comprising 5 mg linagliptin and 10 or 25 mg empagliflozin.

Linagliptin and empagliflozin are known active compounds which improve glycaemic control. Linagliptin belongs to the family of DPP-IV inhibitors, a group of compounds that control glycaemia by increasing the levels of GLP-1 (glucagon-like peptide 1), a bioactive peptide that reduces glucagon secretion and is rapidly degraded by the enzyme DPP-IV. Empagliflozin is a SGLT2 inhibitor, i.e. a compound that controls glycaemia by inducing urinary sugar excretion (patent, paragraphs [0002], [0009], [0198] and [0200]).

In the control of glycaemia, in addition to GLP-1 levels, the level of HbA1c is also an important parameter. HbA1c is a well-known term which refers to the product of a non-enzymatic glycation of the haemoglobin chain. HbA1c levels reflect the average glucose levels of a subject over the preceding four to six weeks (patent, paragraph [0069]). Thus, GLP-1

levels reflect the glycaemic situation in the short term while HbA1c levels reflect the glycaemic situation in the longer term. In addition to reducing glycaemia, high GLP-1 levels also have a beneficial effect on beta-cell regeneration and neogenesis (patent, paragraph [0198]).

7.2 The appellants raised inventive-step objections starting from D2 (or documents with similar content D8 and D20) and D3 as the closest prior art. The party as of right, originally appellant 4, had raised in its statement of grounds of appeal an additional objection starting from linagliptin monotherapy. In its communication in preparation for the oral proceedings on 1 September 2023, the board noted that the latter objection was new and that it was minded not to admit it into the appeal proceedings. At the oral proceedings, the party as of right (then still appellant 4) stated that it had not intended to raise an additional objection. The inventive-step argument starting from linagliptin monotherapy as the closest prior art had only been presented in case the board considered monotherapy to be the closest prior art. No comments on the admittance of the objection were provided. Consequently, the board did not admit the new inventive-step objection under Article 12(4) RPBA 2007.

Thus, the board had to decide on the inventive-step objections starting from D2 and D3 as the closest prior art.

7.3 Starting from D2

7.3.1 D2 discloses selected DPP-IV inhibitors according to the formulae depicted in paragraph [0030]. These DPP-IV inhibitors have exceptional potency and a long-lasting

effect for treating conditions associated with high blood sugar levels (paragraphs [0025] and [0044]). Linagliptin is one of the twelve particularly preferred DPP-IV inhibitors of D2 (paragraph [0032]). Those DPP-IV inhibitors may be combined with other antidiabetic substances, such as SGLT2 inhibitors, to improve the treatment (paragraphs [0045], [0060] and [0061]). Examples of SGLT2 inhibitors are illustrated in paragraph [0067]. They include a generic formula which encompasses empagliflozin.

Example 15 of D2 proposes a clinical study in which a combination of 0.1 to 100 mg of a DPP-IV inhibitor and 0.5 to 1000 mg of a SGLT2 inhibitor are administered to patients having type-2 diabetes or pre-diabetes. The active compounds may be administered in a free combination or in a fixed combination in a tablet. Example 15 also proposes using the corresponding monotherapies as controls to assess whether combination therapy leads to a significantly greater reduction in glucose levels and/or HbA1c levels. The example does not disclose any specific combination of compounds or experimental results.

7.3.2 It was common ground that the dosage form of claim 1 constitutes a selection within the disclosure of Example 15 of D2 in three respects: i) the selection of linagliptin among the preferred DPP-IV inhibitors, ii) the selection of empagliflozin as the SGLT2 inhibitor, and iii) the selection of particular amounts of linagliptin and empagliflozin.

7.3.3 The technical effect produced by these differences was controversial. Nevertheless, it was not contested that the amounts of linagliptin and empagliflozin selected in claim 1 were within the usual dosages for each

compound and that they were not associated with any particular effect. The gist of the invention was the combination of linagliptin with empagliflozin.

The patent states in paragraphs [0220] and [0221] that the compositions of the invention significantly improve glucose excursion compared with each monotherapy. This effect was demonstrated in an animal model in Example I of the patent. Zucker diabetic fatty (ZDF) rats treated with 1 mg/kg linagliptin or 3 mg/kg empagliflozin (see Compound I.3, paragraph [0083]), or a combination of both, received an oral glucose load. Blood glucose excursion was measured over 180 minutes following the glucose challenge. The results were presented in Figure 3 and discussed in paragraph [0226]: linagliptin reduced glucose excursion by 56%, empagliflozin did so by 51%, and their combination by 84%. The latter reduction in glucose excursion was considered statistically significant compared with each monotherapy.

In its reply to the statements of grounds of appeal (page 9, last paragraph to page 10, second paragraph), the respondent noted that this effect was overadditive since the cumulative effect of reducing glucose excursion by 56% and 51% was expected to be 78%. This calculation was not disputed by the appellants.

Additional evidence in support of a technical effect was presented in post-published experimental reports D62 and D64. These showed that the combination of linagliptin with empagliflozin increased GLP-1 levels in an overadditive manner.

In D62, ZDF rats received a daily oral dose of 3 mg/kg linagliptin and 10 mg/kg empagliflozin for four weeks.

The effect on GLP-1 was compared with the baseline and each of the monotherapies. It was observed that linagliptin increased GLP-1 concentration in about 19 pM compared with the baseline, while empagliflozin had essentially no effect. The combination of linagliptin with empagliflozin increased GLP-1 concentration in about 42 pM compared with the baseline. This result demonstrated an overadditive effect on GLP-1 concentration that was statistically significant (p-values below 0.005, see Tables 1:2 and 1:3).

In D64, ZDF rats received an oral daily dose of 3 mg/kg linagliptin or 30 mg/kg empagliflozin, or a combination of both, for five days. The effect of the combination on GLP-1 concentration was compared with the baseline and each of the monotherapies. In all cases, GLP-1 concentrations were measured at three points in time: two hours after dosing on day 2, 23 hours after dosing on day 4, and 47 hours after dosing on day 7 (the last dose was on day 5). The results in Tables 1 and 2 of D64 show that empagliflozin had a minimum effect on GLP-1 concentrations compared with the baseline. However, the combination of linagliptin with empagliflozin increased GLP-1 concentrations considerably more than linagliptin alone, especially two hours after dosing (day 2) and 23 hours after dosing (day 4). The effect was nearly lost 47 hours after dosing (day 7). Thus, D64 demonstrates an overadditive effect of the combination on GLP-1 levels. This effect was statistically significant (p-values below 0.005, see Table 2).

7.3.4 Appellant 3 argued that the dosages in claim 1 were 25 to 65 times lower than in D62 and D64. Therefore, the

technical effect shown in D62 and D64 could not be expected for the combinations in claim 1.

D62 and D64 disclose tests carried out in an animal model. According to D17 (page 476, right-hand column, second paragraph) and D23 (page 1177, last paragraph), an oral daily dose of 5 mg linagliptin is safe and effective for controlling glycaemia in humans. In addition, the appellants argued in the context of obviousness that the usual oral daily dose of empagliflozin for controlling glycaemia was 10 to 50 mg, as disclosed in Example III of D26 (page 37, dosage of active ingredient A). Therefore, the board sees no reasons to doubt that the effect on GLP-1 shown in the animal model of D62 and D64 can be transposed to humans at the doses defined in claim 1, which are known to be safe and effective for controlling glycaemia.

7.3.5 The appellants also argued that, in accordance with decision G 2/21, the overadditive effect on GLP-1 levels assigned to the combination of linagliptin and empagliflozin could not be taken into account for the assessment of inventive step. The effect was not derivable from the application as filed or from common general knowledge, since empagliflozin could not be expected to have an effect on GLP-1 levels. Empagliflozin was a SGLT2 inhibitor and its mode of action was known to be the induction of urinary sugar excretion.

The board disagrees. Decision G 2/21 establishes that post-published evidence of a technical effect may be taken into consideration if the skilled person, having common general knowledge in mind, and based on the application as originally filed, would derive said effect as being encompassed by the technical teaching

and embodied by the same originally disclosed invention.

The application as filed was generally directed to the combination of linagliptin with a SGLT2 inhibitor for improving glycaemic control compared with monotherapy (see e.g., page 4, lines 11 to 15). The mode of action of linagliptin and SGLT2 inhibitors was common general knowledge and it was also disclosed in the application as filed (page 1, lines 20 to 25; page 2, line 33 to page 3, line 5; page 48, lines 19 to 24): linagliptin increases GLP-1 levels and SGLT2 inhibitors promote glucose urinary excretion. Thus, the application was directed to the control of glycaemia by increasing both GLP-1 levels and glucose excretion. As argued by the respondent, the fact that the combination of linagliptin and empagliflozin increases GLP-1 levels in an overadditive manner does not change the nature of the effect assigned to the combination of the invention. It merely relates to a difference in intensity, which becomes relevant when quantification is necessary for comparison with the closest prior art. Therefore, the effect shown in D62 and D64 was encompassed by the teaching of the application as filed.

In addition, Example I of the application shows that the combination of linagliptin with empagliflozin produces a postprandial overadditive excursion of glucose. This necessarily means that there is a synergistic interaction between linagliptin and empagliflozin, i.e. linagliptin enhances the effect of empagliflozin or empagliflozin enhances the effect of linagliptin, or both. Two of these three options imply that empagliflozin enhances the effect of linagliptin on GLP-1 levels. Therefore, in the light of common

general knowledge and Example I of the application as filed, the skilled person would consider it likely that the overadditive glucose excursion observed in Example I of the patent was at least partially due to an increase in the effect on GLP-1 levels compared with linagliptin monotherapy. Therefore, the effect shown in D62 and D64 was embodied by Example I in the application as filed. D62 and D64 merely confirmed this effect.

Consequently, decision G 2/21 does not preclude taking into account the overadditive effect on GLP-1 levels produced by the combination of linagliptin and empagliflozin in claim 1, as confirmed by D62 and D64.

7.3.6 The appellants also argued that the clinical tests in D43, D44 and D45 were more relevant than the tests in the animal model in D62 and D64. The clinical tests showed that the effect of the combination in claim 1 on HbA1c levels was not surprising. At best, it was higher than monotherapy, as could be expected for a combination of two compounds acting by different mechanisms. But more importantly, D43 showed (conclusions in the abstract) that when 5 mg linagliptin were combined with 25 mg empagliflozin, the effect of the combination was not superior to that of empagliflozin alone. Therefore, the combination in claim 1 did not provide any therapeutic improvement when treating conditions related to high glucose levels.

The board agrees with the appellants that D43, D44 and D45 do not show any unexpected effect of the combination of claim 1 on HbA1c levels. However, this does not mean that the overadditive effect on GLP-1 levels shown in D62 and D64 does not translate into a

therapeutic benefit. GLP-1 and HbA1c relate to different aspects of glycaemic control. As taught in the application as filed (page 48, fourth paragraph), high GLP-1 levels are known to promote beta-cell regeneration and neogenesis. This was also common general knowledge (see e.g. D63, Figure 3 and page 2148, left-hand column, last full sentence). Therefore, a lack of an unexpected effect on HbA1c levels does not render the overadditive effect on GLP-1 levels irrelevant.

7.3.7 The appellants were also of the opinion that the respondent should have demonstrated by way of comparative examples that the effect of the claimed combination on GLP-1 levels was advantageous over other combinations encompassed by Example 15 of D2.

The board disagrees. Example 15 does not disclose any particular combination of a DPP-IV inhibitor with a SGLT2 inhibitor, or experimental results. It merely conveys the general expectation that the combination of two active ingredients acting by two different mechanisms may result in an effect superior to either monotherapy. Example 15 does not disclose or suggest any overadditive effect. In contrast, the respondent showed in the application as filed and in D62 and D64 that the combination of a particular DPP-IV inhibitor according to D2 with a particular SGLT2 inhibitor enhances GLP-1 levels in an overadditive manner. This technical effect was not disclosed in Example 15 and there is no basis for assuming that it generally arises across the combinations encompassed therein. Furthermore, given the generic nature of Example 15 and its lack of experimental data, it would not be reasonable to ask the respondent to provide evidence of the fact that a number of unspecified compositions

covered by the example do not exhibit an effect that is not even disclosed therein.

Therefore, the board sees no need for the respondent to provide comparative examples. A discussion of the tests in D64 involving combinations of empagliflozin with sitagliptin and vildagliptin appears superfluous, especially considering that sitagliptin and vildagliptin are not DPP-IV inhibitors according to D2 (see the formulae in paragraph [0030]).

7.3.8 In summary, the board acknowledges that the technical effect produced by the features which distinguish the subject-matter of claim 1 from the closest prior art is an improvement in the control of postprandial glycaemia due to an overadditive production of GLP-1. It has not been disputed that high GLP-1 levels are known to promote beta-cell regeneration and neogenesis (see e.g. D63, Figure 3 and page 2148, left-hand column, last full sentence; and the application as filed, page 48, fourth paragraph).

7.3.9 On the basis of this technical effect, the objective technical problem is to provide an improved pharmaceutical dosage form for reducing glycaemia.

7.3.10 The solution proposed in claim 1 was not obvious. It has not been disputed that the combination of antidiabetic agents acting by different mechanisms was a common strategy for treating type-2 diabetes, as taught in D56, D57 and D58. However, none of the documents cited by the appellants suggests that the combination of linagliptin with empagliflozin may reduce glycaemia in such a way that GLP-1 levels are particularly high, with the consequent benefit for beta-cell regeneration and neogenesis.

In this connection, the appellants referred to D2 alone or the combination of D2 with D3, D24, D26, D33 and D74.

D2 alone could not lead to the claimed solution. It discloses linagliptin as one of the 12 preferred DPP-IV inhibitors. Empagliflozin, albeit not singled out, is encompassed by the formula at the bottom of page 7, left-hand column. However, D2 does not suggest combining linagliptin with empagliflozin, nor does it provide any indication of the particular advantages that this combination provides on GLP-1 production.

D3 discloses new SGLT2 inhibitors for treating metabolic conditions (page 2, first and second paragraphs). Empagliflozin is one of the 17 particularly preferred compounds (page 26, compound 3). D3 suggests combining the new SGLT2 inhibitors with a long list of other active compounds, including DPP-IV inhibitors (page 44, line 3). The combination of D2 with D3 does not suggest combining linagliptin with empagliflozin at all, let alone in order to produce unexpectedly high levels of GLP-1.

D24 teaches that linagliptin is advantageous over other DPP-IV inhibitors, namely vildagliptin, sitagliptin, saxagliptin and alogliptin, for treating type-2 diabetes (abstract). This teaching does not go beyond that in D2, i.e. that linagliptin is a preferred DPP-IV inhibitor. The combination of D2 with D24 would not have led the skilled person faced with the problem posed to combine linagliptin with empagliflozin.

D26 is directed to the combination of SGLT2 inhibitors with other antidiabetic compounds for treating

metabolic disorders (abstract and page 4, last paragraph). Empagliflozin is one of the 17 SGLT2 inhibitors proposed for combination (page 5, compound 3). Example III discloses combinations of specific SGLT2 inhibitors, including empagliflozin, with other antidiabetic compounds. None of the combination partners is a DPP-IV inhibitor. Therefore, the combination of D2 with D26 does not suggest combining linagliptin with empagliflozin to solve the problem posed, either.

D33 states that the combination of DPP-IV inhibitors with other antidiabetic compounds provides a potential opportunity for synergy (page 4138, right-hand column, fourth paragraph). Such a generic statement did not provide the skilled person with a reasonable expectation that the particular combination of linagliptin with empagliflozin is synergistic.

D74 teaches that the effect of linagliptin on HbA1c and GLP-1 is superior to that of vildagliptin, due to its longer-lasting effect. Once again, this teaching does not go beyond that of D2, which discloses linagliptin as a member of an advantageous subgroup of DPP-IV inhibitors to which vildagliptin does not belong. The combination of D2 with D74 does not suggest the advantageous effect of combining linagliptin with empagliflozin, either.

7.4 Starting from D3

7.4.1 At the oral proceedings before the board, the parties agreed that the inventive-step situation does not change if D3 is taken as the closest prior art instead of D2. Therefore, they did not comment on this matter.

7.4.2 D3 discloses the preparation of new SGLT2 inhibitors for treating metabolic conditions (page 2, first and second paragraphs). Empagliflozin is one of the 17 compounds considered as being particularly preferred (page 26, compound 3). D3 suggests combining the new SGLT2 inhibitors with a long list of other active compounds, including DPP-IV inhibitors such as sitagliptin and vildagliptin (page 44, line 3). The examples in D3 describe the preparation and characterisation of compounds according to the invention and formulations thereof. D3 does not contain any examples or data on biological activity.

7.4.3 The subject-matter of claim 1 differs from D3 in the choice of the active compounds combined and their respective amounts. As set out above in the context of D2 as starting point, these differences bring about a control of postprandial glycaemia based on an overadditive production of GLP-1 which promotes beta-cell regeneration and neogenesis.

7.4.4 The objective technical problem is to provide an improved pharmaceutical dosage form for reducing glycaemia.

7.4.5 The solution proposed in claim 1 was not obvious. The appellants cited D2, D4, D17 and D24 as combination documents, because these documents disclose advantages of linagliptin over other DPP-IV inhibitors.

The appellants' arguments fail since they are based on a definition of the objective technical problem as being an alternative. The fact that linagliptin is an advantageous DPP-IV inhibitor according to D2, D4, D17 and D24, does not suggest that it may be combined with empagliflozin to produce an overadditive effect on

GLP-1 levels. D3 does not suggest any particular combination of empagliflozin. It discloses 17 equally preferred SGLT2 inhibitors and a long list of possible combination partners. D3 does not point to any particular combination, let alone to a combination that provides an advantageous effect on GLP-1.

7.5 Therefore, the board concludes that the subject-matter of claim 1 involves an inventive step. As claim 1 is the sole independent claim, auxiliary request 1 meets the requirements of Article 56 EPC.

8. *Requests for reopening the debate, staying the proceedings and referring questions to the Enlarged Board of Appeal*

8.1 At the end of the oral proceedings on 1 September 2023, the board announced its conclusions on the issues discussed and closed the debate on those issues, including the discussion on whether post-published data in D62 and D64 can be taken into account for the assessment of inventive step starting from D2 and D3. The oral proceedings were adjourned because the question of whether D1 was state of the art for the assessment of inventive step remained open. The answer to this question depended on the outcome of the referral in consolidated cases G 1/22 and G 2/22, which were pending before the Enlarged Board of Appeal at that time.

Once the decision on cases G 1/22 and G 2/22 was handed down, the board concluded that D1 could not be considered for the assessment of inventive step since the claimed priority was valid. Therefore, a decision could be issued in writing without the need to hold further oral proceedings. The board informed the

parties accordingly and gave them two months to submit their comments or requests on issues on which the debate had not been closed (see point XI above).

None of the parties contested the board's conclusion that D1 could not be considered for the assessment of inventive step. However, appellants 1 and 5 requested that the debate on inventive step starting from D2 and D3 be reopened because, in the meantime, Board 3.3.04 had taken a decision at oral proceedings in related appeal case T 314/20, which allegedly contradicted the conclusion of the present board at the end of the oral proceedings on 1 September 2023. Appellant 1 also requested that the proceedings be stayed until the written reasoned decision in case T 314/20 be issued or, alternatively, that questions on the interpretation of decision G 2/21 be referred to the Enlarged Board of Appeal.

According to appellants 1 and 5, the contradictory point between decision T 314/20 and the board's conclusions at the end of the oral proceedings on 1 September 2023 was whether decision G 2/21 allowed the consideration of the post-published data in D62 and D64 for the assessment of inventive step.

8.2 Article 15(5) RPBA 2020 stipulates that when a case is ready for decision during oral proceedings, the chair shall state the final requests of the parties and declare the debate closed. No submissions may be made by the parties after the closure of the debate unless the board decides to reopen the debate.

This provision confirms the view of the Enlarged Board of Appeal in decision R 10/08 (Reasons 8), referring to decision G 12/91 (Reasons 3), that the last moment at

which the parties may still make submissions, as far as oral proceedings are concerned, is the closing of the debate. Once the debate has been closed, further submissions by the parties must be disregarded unless the board allows the parties to present comments in writing or decides to reopen oral proceedings for further substantive debate of the issues. The debate should only be reopened in exceptional cases.

8.3 A main consideration for reopening the debate is whether the parties had sufficient opportunity to comment on the grounds and evidence on which the decision is based (Article 113(1) EPC).

At the oral proceedings on 1 September 2023, the inventive step of the subject-matter of auxiliary request 1 starting from D2 and D3 was discussed. In that context, the parties were heard on whether decision G 2/21 allowed the consideration of the post-published data in D62 and D64. After deliberation, the board announced its conclusion that the subject-matter of auxiliary request 1 was inventive. In addition, as recorded on page 5 of the minutes, the board indicated that in arriving at this conclusion it had considered that the combination of compounds in claim 1 produced an unexpected effect on GLP-1 levels. In other words, the post-published evidence in D62 and D64 had been taken into account. Before closing the debate, the board gave the parties the opportunity to comment. There were no comments. The parties did not complain that they had not been sufficiently heard and they did not requested time to react to the board's conclusions, either. The earliest request to reopen the debate was filed more than three months after the oral proceedings.

Therefore, the parties' right to be heard was respected and there were no exceptional reasons for reopening of the debate.

8.4 Appellant 5 argued that the board's conclusion that the data in D62 and D64 could be taken into account was based on an argument raised for the first time by the board at the oral proceedings on 1 September 2023. Appellant 5 had countered the argument with legal reasons, but these were rejected by the board. Allegedly, the same argument was subsequently heard in full, i.e. including legal and technical reasons, by Board 3.3.04 in appeal case T 314/20. Board 3.3.04 came to the conclusion, at the oral proceedings before it, that D64 could not be taken into account. Therefore, appellant 5 considered it justified that the debate be reopened for the present board to hear the technical reasons put forward before Board 3.3.04.

This argument is not convincing. Irrespective of whether the board's reasons to take D62 and D64 into account were discussed for the first time during the oral proceedings on 1 September 2023, appellant 5 had the opportunity to present its technical arguments at those oral proceedings. If appellant 5 needed time to reconsider its case after the board's conclusion on the consideration of D62 and D64, it could have requested this before the debate was closed. However, no requests or comments were made when the board gave the parties the opportunity to do so before closing the debate. The request to be heard on additional arguments was made more than three months after the oral proceedings.

8.5 Appellant 1 and appellant 5 also argued that a reopening of the debate was justified to avoid divergent case law, since Board 3.3.04 had decided in

related appeal case T 314/20 that decision G 2/21 did not allow taking D64 into account. According to appellant 1, at least these appeal proceedings should be stayed until the written reasoned decision in appeal case T 314/20 be issued. In light of that reasoning, the board could reconsider its position and reopen the debate. Furthermore, if the proceedings were not stayed and the debate was not reopened, in view of the diverging views of Board 3.3.04 and the present board, the latter should refer questions to the Enlarged Board of Appeal on the interpretation of decision G 2/21.

These arguments are not convincing. A decision by a different board in a different case does not constitute exceptional circumstances justifying the reopening of the debate. Even if the appeal cases concern closely related subject-matter, the decision in one appeal case is not binding on the other. This is particularly true considering that, as acknowledged by appellant 5, the case presented before Board 3.3.04 in appeal case T 314/20 was not the same as the one presented in the case at hand, at least with respect to technical arguments.

Furthermore, in the absence of exceptional circumstances to reopen the debate, the board sees no reason to stay the appeal proceedings until the written reasoned decision in appeal case T 314/20 is issued. On this point, appellant 1 cited Article 20(1) RPBA 2020 without further explanation. This provision refers to the interpretation of the Convention in an earlier decision by any board, which is not the matter of dispute in these proceedings. Therefore, Article 20(1) RPBA 2020 is irrelevant to the present case.

The referral of questions to the Enlarged Board of Appeal is not justified either, simply because the only purpose of such a referral would be to reopen the debate. As submitted by appellant 5, the case presented in appeal case T 314/20 was not the same as the one presented in the case at hand. The allegation that the two boards have reached a different conclusion on identical facts is not convincing.

8.6 Therefore, the board rejected the requests to reopen the debate, stay the appeal proceedings and refer questions to the Enlarged Board of Appeal.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent in amended form with claims 1 to 14 of auxiliary request 1 as filed with the reply to the statements of grounds of appeal, and a description and drawings to be adapted thereto, if necessary.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated