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**Datasheet for the decision  
of 12 March 2026**

**Case Number:** T 0779/24 - 3.3.07

**Application Number:** 16777058.5

**Publication Number:** 3280416

**IPC:** A61K31/519, A61K9/10,  
A61P25/18, A61P25/24, A61K9/00

**Language of the proceedings:** EN

**Title of invention:**

DOSING REGIMEN FOR MISSED DOSES FOR LONG-ACTING INJECTABLE  
PALIPERIDONE ESTERS

**Patent Proprietor:**

Janssen Pharmaceutica NV

**Opponents:**

Hexal AG  
df-mp Dörries Frank-Molnia & Pohlman  
STADA Arzneimittel AG

**Headword:**

Dosing regimen for long-acting Paliperidone esters / JANSSEN

**Relevant legal provisions:**

RPBA 2020 Art. 12(6) sentence 2, 12(4)  
EPC Art. 83, 56

**Keyword:**

Late-filed evidence - admitted (yes)

Claim interpretation - description taken into consideration

Sufficiency of disclosure - main request (yes)

Inventive step - main request (yes)

**Decisions cited:**

G 0003/14, G 0001/24, G 0002/21, T 0601/02



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Case Number: T 0779/24 - 3.3.07

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.07**  
**of 12 March 2026**

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**Decision under appeal:**            **Decision of the Opposition Division of the European Patent Office posted/electronically transmitted on 31 May 2024 revoking European patent No. 3280416 pursuant to Article 101(3) (b) EPC.**

**Composition of the Board:**

**Chairman**            A. Usuelli  
**Members:**            J. Lécaillon  
                          Y. Podbielski  
                          E. Duval  
                          A. Jimenez

## **Summary of Facts and Submissions**

- I. European patent 3 280 416 (hereinafter "the patent") was granted on the basis of 10 claims. Independent claims 1 and 5 of the patent as granted related to an injectable paliperidone palmitate depot for use in treating a patient in need of psychiatric treatment selected from psychosis, schizophrenia, or bipolar disorder that has been treated with a 3-month injectable paliperidone palmitate depot (PP3M), wherein said patient missed either for a period of four to nine months, or for a period of nine months or longer, the next scheduled maintenance dose of the 3-month injectable paliperidone palmitate depot, characterised by a specific dosing regimen of monthly and 3-month formulations of paliperidone.
- II. Eight oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step and was excluded from patentability according to Article 53(c) EPC, it was not sufficiently disclosed and it extended beyond the content of the application as originally filed.
- III. Opponent 2 withdrew their opposition on 14 December 2022.
- IV. The opposition division took the decision to revoke the patent. This decision was based on a main request as well as three auxiliary requests.
- V. The decision of the opposition division, posted on 31 May 2024, cited *inter alia* the following documents:

D1: Berwaerts *et al.*, JAMA Psychiatry, Vol. 72 (8), pages 830-839, 29 March 2015

D1b: Redacted Clinical Protocol for Journal Use, Protocol R092670PSY3012; Phase 3, AMENDMENT INT-4 R092670 (paliperidone palmitate), 25 July 2013

D1c: Berwaerts *et al.*, JAMA Psychiatry, 29 March 2015, Supplementary Online Content

D2: INVEGA<sup>®</sup> SUSTENNA<sup>®</sup> Patient Leaflet 3657038 (revised 11/2014)

D4: US 2011/0105536 A1 (5 May 2011)

D5: FDA approved full prescribing information for INVEGA TRINZA<sup>™</sup>, reference ID: 3755541 (revised 05/2015)

D19: Summary of product characteristics for TREVICTA<sup>®</sup>

D20: EMA Assessment report for TREVICTA<sup>®</sup>, 1 April 2016

D30: Product label for RISPERDAL<sup>®</sup>, revised 08/2007

VI. The opposition division decided in particular as follows:

- (a) The objection of double patenting under Article 125 EPC was not admitted into the opposition proceedings.
- (b) The priority date of P2 was validly claimed, so that D5 and D6 did not form part of the prior art relevant under Article 54(2) EPC.
- (c) The main request did not contravene Article 53(c) EPC.
- (d) The time period of 4 to 9 months recited in claim 1 of the main request was to start from the last administration of PP3M.

(e) The main request met the requirements of Articles 83 and 54 EPC.

(f) The main request and auxiliary requests 1 to 3 did not meet the requirements of Article 56 EPC.

VII. The patent proprietor (appellant) lodged an appeal against the above decision of the opposition division.

VIII. With their statement setting out the grounds of appeal the appellant defended their case on the basis of the main request or one of the auxiliary requests 1 to 3 filed during the opposition proceedings on 24 January 2024 and resubmitted with the statement setting out the grounds of appeal.

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

Claim 1 of the main request read as follows:

"1. An injectable paliperidone palmitate depot for use in treating a patient in need of psychiatric treatment selected from psychosis, schizophrenia, or bipolar disorder that has been treated with a 3-month injectable paliperidone palmitate depot, wherein said patient misses for a period of more than or equal to four months and up to nine months the next scheduled maintenance dose of the 3-month injectable paliperidone palmitate depot, by a dosing regimen comprising:

(1) administering intramuscularly in the deltoid muscle of said patient a first reinitiation loading dose of a monthly injectable paliperidone palmitate depot;

(2) administering intramuscularly in the deltoid muscle of said patient a second reinitiation loading dose of

the monthly injectable paliperidone palmitate depot on about the 4th day to about the 12th day after administering said first reinitiation loading dose; and

(3) administering intramuscularly in the deltoid or gluteal muscle of said patient the reinitiation 3-month formulation of paliperidone palmitate in the range of about 175mg eq. to about 525 mg eq. on about the 23rd day to about the 37th day after administering the second reinitiation loading dose of the monthly injectable paliperidone palmitate wherein said first and second reinitiation loading doses and the reinitiation 3-month formulation of paliperidone palmitate dose are selected from the table below based on the amount of the missed dose

Missed PP3M dose	Administer PP1M, two doses (into deltoid muscle)		Then administer PP3M (into deltoid or gluteal muscle) Reinitiation 3-month formulation dose
	First Reinitiation Dose	Second Reinitiation Dose	
175 mg eq.	50 mg eq.	50 mg eq.	175 mg eq.
263 mg eq.	75 mg eq.	75 mg eq.	263 mg eq.
350 mg eq.	100 mg eq.	100 mg eq.	350 mg eq.
525 mg eq.	100 mg eq.	100 mg eq.	525 mg eq.

”

The remaining claims 2 to 6 of the main request were dependent claims further specifying the treated condition.

IX. The following item of evidence relevant for the present decision was filed by the appellant with their statement setting out the grounds of appeal (D35):

D35: Urso *et al.*, European Review for Medical and Pharmacological Sciences, 2002, 6: 33-44

- X. Appellants-opponents 1, 4, 5 and 7 withdrew their oppositions on 6 March 2026, 24 February 2026, 10 March 2026 and 11 March 2026, respectively.
- XI. Oral proceedings were held before the Board on 12 March 2026. The respondent-opponent 3 did not attend the oral proceedings as announced with the letter dated 5 March 2026.
- XII. The final requests of the parties were the following:
- (a) The appellant requested that the decision under appeal be set aside and the patent be maintained on the basis of the main request or one of the auxiliary requests 1 to 3 filed during the opposition proceedings on 24 January 2024 and filed again with the statement setting out the grounds of appeal.
- They also requested that the objection of double-patenting not be admitted into the proceedings.
- (b) The respondents-opponents 6 and 8 requested that the appeal be dismissed such that the patent be revoked.
- Respondent-opponent 8 further requested that D35 not be admitted into the appeal proceedings.
- XIII. The respondent-opponent 3 did not make any substantive submission in the appeal proceedings.
- XIV. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:
- (a) Admittance of D35

D35 was to be admitted because it was directly responsive to the impugned decision regarding the flaw in calculating PP3M's half-life, it was not complex, and was filed at the earliest opportunity (Article 12(4) RBPA).

(b) Objection of double patenting

The opposition division's decision not to admit the objection of double patenting was correct and no specific circumstances were invoked to admit this objection in the appeal proceedings.

(c) Claim interpretation

In line with G 1/24 and in view of the overall disclosure of the description of the patent, the time period for which the patient misses the next scheduled maintenance dose of the 3-month injectable paliperidone palmitate depot (PP3M) defined in claim 1 of the main request was to be understood as starting from the time point at which the last PP3M maintenance dose was administered.

(d) Sufficiency of disclosure

The subject-matter of the claims of the main request was sufficiently disclosed. The claimed therapeutic effect was rendered credible in view of common general knowledge on the efficacy of paliperidone palmitate and in view of the *in silico* data provided in the application as originally filed regarding the claimed dosage regimen.

(e) Inventive step

D1, which related to a clinical trial on the treatment of schizophrenia patients with PP3M, represented the closest prior art since it was the only cited document relating to PP3M treatment. The claimed subject-matter differed from the disclosure of D1 in that the patient missed a PP3M dose so that a re-initiation dosage regimen was required. The claimed dosage regimen allowed to restore PP3M treatment in patients having missed their PP3M for a period of 4 to 9 months since the last injection. The period of time of the missed dose represented a contribution to the art and should not be included in the formulation of the objective technical problem. The objective technical problem to be solved resided therefore in the provision of a dosage regimen which was able to treat a psychiatric patient who had previously been treated with PP3M but who had missed one or more doses of PP3M. The dosage regimen of claim 1 of the main request was not obvious in light of the cited prior art. D1 did not provide any indication on how to proceed in case of a missed dose. Moreover, the skilled person would not have turned to documents relating to re-initiation of monthly paliperidone palmitate injection (PP1M) treatment after a missed dose such as D4, because of the significant differences in the PK properties between PP1M and PP3M. However, even if the skilled person had taken D4 into consideration, they would not have arrived at the present dosage regimen. There was no teaching of the period of time since the last administered dose during which re-initiation was to be performed in any of the cited prior art. Furthermore, there was no incentive in the prior art to administer only two initiation PP1M doses followed by a PP3M maintenance dose.

Should D4 be considered a suitable starting point for the assessment of inventive step, the claimed subject-matter would still involve an inventive step. The claimed subject-matter differed from the disclosure of D4 in that patients were treated with PP3M instead of PP1M before the missed dose, in the time period of missing the dose and in the nature of the re-initiation dosage regimen. As when starting from D1, the claimed dosage regimen allowed to restore PP3M treatment in patients having missed their PP3M for a period of 4 to 9 months since the last injection. It followed that the same objective technical problem was to be formulated as in the approach starting from D1. For the same reasons as detailed in this previous approach, D4 either alone or taken in combination with common general knowledge and/or D1 did not lead to the re-initiation regimen of claim 1 of the main request.

Hence, the main request met the requirements of Article 56 EPC.

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

(a) Admittance of D35

According to respondent-opponent 8, D35 was not to be admitted into the appeal proceedings because it should have been filed earlier (Article 12(6), 2<sup>nd</sup> paragraph RPBA). It concerned the determination of a drug's pharmacokinetics (PK) parameters such as half-life and the issue of the determination of PP3M half-life had already been raised at the outset of the opposition proceedings and discussed by the opposition division in their preliminary opinion.

(b) Objection of double patenting

According to respondent-opponent 8, claim 1 of the main request was identical in scope with claim 1 of the patent EP 3 744 326, filed as a divisional application of the present patent and granted on 6 December 2023. The main request was therefore unallowable under the principle of double patenting (Article 125 EPC).

(c) Claim interpretation

The wording of claim 1 of the main request was linguistically clear. The use of the verb "miss" together with the reference to the "next scheduled maintenance dose" unambiguously indicated that the 4 to 9 month period started from the time point at which the next PP3M maintenance dose was due, which implied a longer time period of 7 to 12 months starting from the last injected dose. In such a case the description could not override the clear claim wording.

(d) Sufficiency of disclosure

According to respondent-opponent 8, the subject-matter of the claims of the main request was not sufficiently disclosed. The skilled person was not in a position to verify the *in silico* results obtained in the patent due to the lack of disclosure of the clinical data and the detailed PK model parameters used as well as of the input data for the simulations.

(e) Inventive step

D4 represented the most appropriate starting point for the assessment of inventive step because it related to the management of missed doses of a paliperidone

palmitate depot formulation. According to respondent-opponent 6, D1 also represented a suitable closest prior art document.

Starting from D1, the claimed subject-matter differed from the disclosure thereof in that the patient missed a PP3M dose so that a re-initiation dosage regimen was required. The claimed dosage regimen allowed to restore PP3M treatment in patients having missed their PP3M for a period of 4 to 9 months since the last injection. The period of time of the missed dose was to be included in the formulation of the objective technical problem because it defined the framework within which the technical effect of restoring the PP3M treatment was achieved. The objective technical problem to be solved resided therefore in the provision of a re-initiation regimen for PP3M treated patients who had missed a dose of PP3M for a period of 4 to 9 months since the last administered PP3M dose. However, according to respondent-opponent 6, even if the time period was not included in the definition of the objective technical problem, the solution would still be obvious as this time period would be determined through routine experimentation. The skilled person would have consulted D4 relating to the management of missed PP1M dose. The skilled person would have deduced that the plasma concentration after having missed a PP3M dose for the time period defined in claim 1 of the main request would be comparable to that after having missed a PP1M dose for the period of 6 weeks to 6 months described in D4. Being aware that the steady-state plasma drug concentrations are comparable in PP1M and PP3M treatment and of the possibility to switch stabilised patients from PP1M to PP3M treatments (see D1), the skilled person would have applied the two loading PP1M doses as described in D4 followed by a

maintenance PP3M dose to solve the problem posed. The claimed solution was therefore obvious starting from D1 in combination with D4 and common general knowledge.

Starting from D4, the claimed subject-matter differed from the disclosure thereof in that patients were treated with PP3M instead of PP1M before the missed dose, in the time period of missing the dose and in the nature of the re-initiation dosage regimen. The objective technical problem could be formulated in the same manner as when starting from D1. The skilled person would have consulted D1 relating to a clinical trial on the treatment of schizophrenia patients with PP3M. For the same reasons as detailed above starting from D1, the skilled person would have applied the two loading PP1M doses as described in D4 followed by a maintenance PP3M dose to solve the problem posed. The claimed solution was therefore obvious starting from D4 in combination with D1 and common general knowledge.

As a result, the main request did not meet the requirements of Article 56 EPC.

## **Reasons for the Decision**

1. Admittance of D35
  - 1.1 Respondent-opponent 8 requested that D35 not be admitted into the appeal proceedings. They argued that this document, which concerned the determination of a drug's pharmacokinetics (PK) parameters such as half-life, should have been filed earlier (Article 12(6), 2<sup>nd</sup> paragraph RPBA). The issue of the determination of PP3M half-life had indeed been raised at the outset of the opposition proceedings (see e.g. notice of opposition of opponent 7, pages 14 and 16) and

discussed by the opposition division in their preliminary opinion (see annex to the communication of the opposition division dated 28 March 2023, section 21.11.1.8). According to respondent-opponent 8, D35 should therefore have been filed at the latest with the reply to said preliminary opinion.

- 1.2 The Board observes that the communication of the opposition division dated 28 March 2023, drew attention in section 21.11.1.8 to a number of issues to be discussed in connection with PK parameters of PP3M. However, the calculation based on the eFigure of D1c and the conclusions drawn therefrom by the opposition division as stated in the impugned decision were not expressed in their preliminary opinion. The Board considers therefore that there were no compelling reasons for the appellant to file D35 already during the opposition proceedings (Article 12(6), 2<sup>nd</sup> paragraph RPBA).
- 1.3 Moreover, as stated by the appellant and not disputed by respondent-opponent 8, D35 was filed at the earliest possible point in time in the appeal proceedings, it is not complex and addresses an issue which led to the decision under appeal.
- 1.4 Hence, D35 is admitted into the appeal proceedings (Article 12(4) RPBA).

*Main request*

2. Objection of double patenting
- 2.1 During the written appeal proceedings respondent-opponent 8 maintained their objection of double patenting under Article 125 EPC raised during the

opposition proceedings, because claim 1 of the main request would be identical in scope with claim 1 of the patent EP 3 744 326, filed as a divisional application of the present patent and granted on 6 December 2023.

2.2 In the impugned decision, the opposition division considered that double patenting was not a ground of opposition and that the amendments to the present main request were not causative of the potential objection of double patenting. Consequently, in line with G 3/14, the issue of double patenting was not to be examined in the opposition proceedings.

2.3 Respondent-opponent 8 did not provide any arguments why the opposition division's reasoning regarding the non-admittance of the objection was not correct. The objection of double-patenting does therefore not form part of the appeal proceedings.

### 3. Amendments and exclusion from patentability

The remaining parties to the proceedings did not raise any objection of lack of compliance with the requirements of Articles 123(2) and 53(c) EPC. Furthermore, the Board sees no reason to overturn the decision the opposition division finding that the main request fulfilled the requirements of these articles.

### 4. Claim interpretation

4.1 The understanding of the feature mandating that the "patient misses for a period of more than or equal to four months and up to nine months the next scheduled maintenance dose of the 3-month injectable paliperidone palmitate depot" in claim 1 of the main request was a key issue in the present case.

- 4.2 In the impugned decision, the opposition division considered that from the reading of the claim itself two alternative interpretations of the time period of 4 to 9 months were possible, namely that the period was to start from:
- (i) the time point at which the last PP3M maintenance dose was administered, or
  - (ii) the time point at which the next PP3M maintenance dose would have been administered.

Turning to the description, the opposition division concluded that the skilled person would be in a position to clarify that the above interpretation (i) was meant.

- 4.3 In their written submissions, the respondents-opponents 6 and 8 disputed this conclusion. They considered that the claim wording was linguistically clear. According to them, the use of the verb "miss" together with the reference to the "next scheduled maintenance dose" (emphasis added) unambiguously indicated that the 4 to 9 month period started from the time point at which the next PP3M maintenance dose was due, which implied a longer time period of 7 to 12 months starting from the last injected dose. The respondents-opponents 6 and 8 considered that in such a case the description could not override the clear claim wording.

- 4.4 The Board concurs with the opposition division that the wording of present claim 1 with respect to the feature of the time period wherein the patient misses the regular PP3M dose is ambiguous and that, when reading claim 1 in isolation, both interpretations (i) and (ii) defined above may apply.

Contrary to the respondents view, and as stated by the opposition division (see impugned decision point 27.5.8.3.6), the reference in the present feature to the "next scheduled maintenance dose" (emphasis added) does not necessarily mean that the starting time point for the period defined in present claim 1 is the time point at which the next PP3M maintenance dose would have been administered. The treatment with PP3M is a chronic one, which can be seen as a succession of treatment phases of 3 months. Hence, claim 1 can also be read in the sense that the patient of claim 1 misses the periodicity of the treatment, in which case the starting time point for the period defined in present claim 1 is the time point at which the last PP3M maintenance dose was administered.

- 4.5 As argued by the appellant, when consulting the description to interpret present claim 1 in accordance with G 1/24 (see order), it appears that the overall description considers the time point at which the last PP3M maintenance dose was administered as the starting point for the period defined in the claimed dosage regimen (see paragraphs [0024] to [0027] constituting the "Missed Doses" section and specifying the time intervals in each headings and in the text as "since the last injection"; Example 1, paragraph [0076] specifying a duration "since the last dose" and Table 5 mentioning the "time interval of missed dose"; paragraph [0085] and Figures 4A to 4C specifying a duration "after last dose").

The teaching of these passages in this respect was not disputed by the respondents. Furthermore, the respondents did not point to any passage of the description which would indicate a different starting

time point for the definition of the time periods of the claims.

4.6 It follows that, when consulting the description, as required under G 1/24, the skilled person would have no doubt that the time period defined in present claim 1 is to be interpreted as starting from the time point of administration of the last PP3M maintenance dose.

5. Sufficiency of disclosure

5.1 In their written submissions, respondent-opponent 8 contested that the claimed invention was sufficiently disclosed.

5.2 Present claim 1 is worded as a purpose limited product claim and relates to a specific dosage regimen for the re-initiation of PP3M treatment in patients in need of a treatment of psychosis, schizophrenia or bipolar disorder and who have been treated with PP3M but did not receive their scheduled PP3M dose for 4 to 9 months since the last administered dose. It is a general principle when assessing compliance with the requirements of Article 83 EPC that, when the therapeutic effect is a functional feature of the claims, the suitability of the claimed product and/or dosage regimen to achieve said effect must be disclosed.

5.3 In the present case, as argued by the appellant, paliperidone palmitate was a known antipsychotic drug which previously received regulatory approval for the treatment of schizophrenia (see the patent, paragraphs [0004] to [0006] and D2). Furthermore paliperidone was known to be the major active metabolite of risperidone, itself known to be efficacious in the treatment of

bipolar disorders (see patent paragraph [0003] and D30). Hence, the suitability of PP3M in the treatment of the claimed diseases was established from common general knowledge and the prior art.

- 5.4 Furthermore, as also explained by the appellant, the present patent provides results of *in silico* simulations of paliperidone plasma concentrations at various time intervals and of the effect of the claimed dosage regimen in restoring the concentrations achieved before missing a dose for the time period defined in present claim 1 (see example 1, Figure 4B). As stated in the patent, these simulations were based on a population pharmacokinetics model which was constructed using data from clinical studies (see paragraph [0073]). Details on the PK models, calculation models and computer software used are provided in the patent (see paragraphs [0074] and [0075]).
- 5.5 Respondent-opponent 8 brought forward that the lack of disclosure of the clinical data and the detailed PK model parameters used as well as the input data for the simulations rendered a verification of the results obtained in example 1 and Figure 4B impossible.
- 5.6 The Board concurs with the appellant, that, in the present case, Article 83 EPC only requires that the claimed dosage regimen be demonstrated as suitable for achieving the claimed therapeutic effect. There is no absolute requirement for experimental data (see e.g. G 2/21, reasons 77 and T 601/02 reasons 9.). In the present case, the *in silico* simulations, which are built on PK data obtained from clinical studies, substantiate this suitability.

Concerning reproducibility of the claimed invention, as argued by the appellant, the patent provides the details of the dosage regimen and of appropriate PP1M and PP3M formulations and their preparation (see paragraphs [0037] to [0067] and example 1). The claimed invention is therefore reproducible. Moreover, the details provided in the patent about how the results of example 1, which support the suitability of the dosage regimen in the claimed treatment, were obtained are considered sufficient to render these results credible.

5.7 During oral proceedings, appellant-opponent 8 indicated that, in view of the conclusion reached regarding the claim interpretation, they no longer relied on their objection raised under Article 83 EPC. Hence, the further argument of appellant-opponent 8 regarding a reinstatement in the case of a time period of 7 to 12 months since the last administered PP3M dose is no longer relevant.

5.8 Accordingly, the main request complies with the requirements of Article 83 EPC.

6. Inventive step

6.1 Closest prior art

6.1.1 The patent relates to a dosage regimen for the re-initiation of PP3M treatment in patients in need of a treatment of psychosis, schizophrenia or bipolar disorder and who have been treated with PP3M but did not receive their scheduled PP3M dose for 4 to 9 months since the last administered dose. PP3M is a formulation that delivers paliperidone palmitate over a period of three months. At the priority date, paliperidone palmitate was also available as a formulation designed

for monthly administration, PP1M (see for instance D10, example 5).

6.1.2 The parties disagreed regarding the choice of the closest prior art. The appellant considered that D1, which related to the treatment of psychiatric diseases with PP3M, represented the closest prior art. The opposition division as well as respondent-opponents 6 and 8 considered that D4, relating to the paliperidone palmitate monthly formulation PP1M, represented a better choice since it addressed the same purpose of restoring a treatment after a patient missed a dose for a given period of time. Appellant-respondent 6 nevertheless considered that D1 might also represent a suitable starting point.

6.1.3 The Board agrees with the appellant, that from a real life point of view, the issue of re-initiation of a treatment with PP3M when a patient missed a dose would arise when concerned with a treatment with PP3M. For this reason, D1 represents a more realistic starting point than D4 which relates to a different formulation. However, both D1 and D4 represent suitable starting points for the assessment of inventive step, so that for inventive step to be acknowledged, the claimed subject-matter must be inventive starting from both documents.

6.2 Starting from D1

6.2.1 D1 reports the successful results of a clinical trial on the treatment of schizophrenia patients with PP3M. The patients received once-monthly PP1M doses in the transition phase and then a single dose (3.5 times the dose of PP1M) of PP3M in the maintenance phase. Stabilized patients were subsequently receiving either

a fixed dose of PP3M or placebo (see Abstract; page 831, right column; and D1c, eTable 1). The formulations were injected either in the deltoid or gluteal muscle.

*Distinguishing feature*

6.2.2 It was common ground that the claimed dosage regimen differs from the one of D1 in that there is no missed dose situation in D1, in particular not for a period of 4 to 9 months since the last PP3M injection, and hence no re-initiation regimen.

*Objective technical problem*

6.2.3 It was undisputed amongst the parties that the claimed dosage regimen allows to restore paliperidone plasma concentrations in patients having missed their PP3M for a period of 4 to 9 months since the last injection, to the steady-state level achieved in stabilised patients before missing a dose and hence restore PP3M treatment (see the patent, Example 1, in particular Figure 4B as well as D19 and D20 reporting the regulatory approval of the claimed dosage regimen for patients receiving PP3M and who missed one or more dose for the presently claimed period of time).

6.2.4 The objective technical problem can therefore be formulated as the provision of a re-initiation regimen for PP3M treated patients who have missed a dose of PP3M for a period of 4 to 9 months since the last administered PP3M dose.

*(Non)-obviousness*

6.2.5 According to the respondents-opponents 6 and 8, the skilled person would have consulted D4 which provides a re-initiation dosage regimen for PP1M patients having missed a dose and, based on this document and common general knowledge, would have arrived at the present re-instatement dosage regimen.

They argued that the concept of re-initiation *per se* was already known from D4 for PP1M and hence not inventive. Furthermore they considered that the specific re-initiation regimen was obvious. The skilled person would have compared the residual concentrations after a missed PP3M dose with those after a missed PP1M dose. Furthermore, the skilled person would be aware that PP3M was developed to deliver at maintenance plasma concentration equivalent to those achieved with corresponding 3.5 lower PP1M dose and that maintenance regimens of PP1M and PP3M were interchangeable at steady state (see D1, Abstract and right-hand column on page 831, D1b section 4.2.1 on pages 22-23 and D1c eTable 1). Hence, the skilled person would have had a reasonable expectation that the re-initiation approach developed for PP1M in D4 would also be successful for PP3M.

Accordingly, in light of the teaching set out in paragraph [0043] of D4, the skilled person would have re-initiated the PP3M treatment after having missed a dose for a period of 4 to 9 months by administering in the deltoid muscle:

- a first PP1M loading dose,
- a second PP1M loading dose the 6<sup>th</sup> to 10<sup>th</sup> day after the first loading dose, and
- a PP3M maintenance dose on the 23<sup>rd</sup> to 37<sup>th</sup> day after the first loading dose,

wherein the two loading doses were the same dosing amount as the stabilized dose prior to the missed dose.

By applying the 3.5 conversion factor between PP3M and PP1M disclosed in D1 (see page 837, left column, 2<sup>nd</sup> full paragraph, 1<sup>st</sup> sentence), the skilled person would have arrived at doses corresponding to the presently claimed ones.

6.2.6 The Board concurs with the respondents that the skilled person would have been aware of the importance of (i) the residual paliperidone plasma concentration after the missed dose and (ii) the necessity to restore plasma concentration of paliperidone corresponding to steady-state levels of paliperidone.

6.2.7 However, the Board is not convinced that the skilled person would have turned to the dosage regimen of D4 relating to the restoration of a PP1M treatment when aiming at restoring PP3M treatment. The two formulations differ in their duration of action, and there is no indication that the pharmacokinetic data derived from PP1M could be extrapolated to PP3M.

6.2.8 Even if one assumes that the skilled person would indeed have turned to D4, it remains that there is no guidance in the prior art on how to adapt the re-initiation regimen for PP1M patients of D4 to PP3M patients. In the absence of any guidance, a variety of different options might have been conceptualized by the skilled person, including:

- a full restoration of treatment with PP1M as disclosed in D4 (*i.e.* two PP1M loading dose and a PP1M maintenance dose) followed by a switch to PP3M treatment (following the scheme of D1 wherein PP1M

stabilised patients are switched to PP3M treatment),

- a similar strategy as in D4 including two loading doses and one maintenance dose but with only PP3M doses, and
- a regimen mixing two PP1M loading doses and a PP3M maintenance dose as suggested by the opponents.

6.2.9 The Board considers that the skilled person would not have found any hint in the prior art towards this last approach.

Contrary to the opinion of the respondent-opponent 8 as stated during the oral proceedings, it is not evident that the PP1M maintenance dose (third dose of PP1M in the re-initiation regimen) of D4 is meant to "resume" the treatment, so that the skilled person willing to solve the problem posed would necessarily apply a PP3M dose at this stage.

D1 teaches that patients having received PP1M treatment during a 12-week transition phase *i.e.* patients stabilised with PP1M may be switched to PP3M taking into account the dose conversion factor (see Abstract). There is no teaching in D1, nor in any other cited prior art, that a patient could successfully be switched from PP1M to PP3M after only two PP1M loading doses, *i.e.* once a plasma concentration which would be desirable for a steady-state treatment has been reached, but before a proper steady-state treatment has actually been instituted. The skilled person would therefore not have had any motivation to modify the re-initiation regimen of D4 by using only two PP1M loading doses and then apply directly a PP3M maintenance dose.

6.2.10 In this context, respondent-opponent 6 argued that the purpose of re-initiation was to restore therapeutic plasma concentrations. Once those concentrations had been restored, there was no technical rationale for repeated administration of PP1M maintenance doses to maintain those therapeutic plasma concentrations for a prolonged period rather than immediately resuming PP3M. On the contrary, maintaining the patient on PP1M would have added complexity and unnecessarily deferred the advantage associated with PP3M, namely reduced dosing frequency. The requirement in the prior art trial (D1) and the (post-published) authorised use of PP3M (D5) for repeated PP1M maintenance dosing before commencing PP3M was explained by the need to confirm tolerability before initiating a long-acting product. That consideration would not apply after a missed PP3M dose, because the patient had already been exposed to, and stabilised on, paliperidone palmitate.

The Board is not convinced by this argument. While it provides an explanation of the possible reasons for the repeated administration of the PP1M maintenance dose before switching to PP3M in the case of the study of D1 (and D5), it is not substantiated by any further evidence. It remains that there was no indication in the prior art at the priority date that PP3M treatment could be immediately administered after only two loading doses of PP1M.

6.2.11 It follows that the subject-matter of claim 1 of the main request is inventive when starting from D1 as closest prior art.

6.3 Starting from D4

6.3.1 D4 discloses *inter alia* a re-initiation dosage regimen for patients treated with PP1M who have missed a PP1M dose for a period of 6 weeks to 6 months (see paragraph [0043]). It includes the administration of a first PP1M loading dose in the deltoid muscle as soon as possible followed by a second PP1M loading dose in the deltoid muscle about 8 days +/- 2 days later and a PP1M maintenance dose in the deltoid or gluteal muscle at about the 30<sup>th</sup> day +/- 7 days after the first loading dose. The first and second dose depend on the stabilized dose prior to the missed dose. Examples of doses are provided in paragraph [0043] of D4.

6.3.2 It was undisputed amongst the parties that the claimed subject-matter differs from the one of D4 in

- the nature of the treatment formulation (PP3M instead of PP1M),
- the period of time of missing the dose (4 to 9 months instead of 6 weeks to 6 months), and
- the specific doses administered including administration of a PP3M maintenance dose instead of a PP1M one.

6.3.3 Having regard to the technical effect and hence the objective technical problem, similar considerations were made by the parties as starting from D1. During the oral proceedings, the respondents agreed that also the arguments provided in the context of the assessment of the obviousness of the solution provided for the main request were similar since they relied on combinations with common general knowledge and/or D1.

6.3.4 Accordingly, for the same reasons as provided under points 6.2.6 to 6.2.10, the subject-matter of claim 1

of the main request is not obvious starting from D4 in combination with D1 and/or common general knowledge.

6.4 Consequently, the main request meets the requirements of Article 56 EPC.

## Order

### **For these reasons it is decided that:**

The decision under appeal is set aside.

The case is remitted to the opposition division with the order to maintain the patent on the basis of the main request filed on 24 January 2024 and a description to be adapted thereto.

The Registrar:

The Chairman:



B. Atienza Vivancos

A. Uselli

Decision electronically authenticated