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Datasheet for the decision of 18 February 2025

Case Number: T 1125/22 - 3.3.04

Application Number: 16175117.7

Publication Number: 3133070

IPC: C07D405/06, A61K45/06, A61K31/4025, A61P35/00

Language of the proceedings: EN

Title of invention:

Eliglustat (GENZ 112638) as inhibitor of glucosylceramide synthase for use in a method of treating Fabry's or Gaucher's disease, the method comprising adjusting the individual therapeutical dose to the P-450 metabolism of the patient

Patent Proprietor:

Genzyme Corporation

Opponents:

Teva Pharmaceutical Industries Ltd.
Accord Healthcare Ltd
Hetero Labs Limited

Headword:

Eliglustat/GENZYME

Relevant legal provisions:

EPC Art. 83

Keyword:
Sufficiency of disclosure - completeness of disclosure (no)

Decisions cited:
G 0002/21, T 0609/02, T 0801/06, T 1592/12, T 0950/13, T 0321/15, T 0391/18, T 2015/20, T 0108/21

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 1125/22 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 18 February 2025

Appellant: (Opponent 2)	Accord Healthcare Ltd Sage House 319 Pinner Road North Harrow Middlesex HA1 4HF (GB)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted on 21 February 2022 concerning maintenance of the European Patent No. 3133070 in amended form.**

Composition of the Board:

Chairwoman M. Pregetter
Members: D. Luis Alves
L. Bühler

Summary of Facts and Submissions

I. European patent EP 3 133 070, entitled "*Eliglustat (Genz 112638) as inhibitor of glucosylceramide synthase for use in a method of treating Fabry's or Gaucher's disease, the method comprising adjusting the individual therapeutic dose to the P-450 metabolism of the patient*", was granted on European patent application No. 16 175 117.7.

II. Three oppositions were filed, invoking the grounds for opposition under Article 100(a) EPC, for lack of inventive step (Article 56 EPC), as well as the grounds for opposition under Article 100(b) and (c) EPC.

III. The opposition division decided that, account being taken of the amendments in the form of the main request, the patent and the invention to which it related met the requirements of the EPC. The opposition division considered objections under Articles 123(2), 83, 54 and 56 EPC.

IV. Opponents 1 and 2 filed appeals against the opposition division's decision.

V. With the statement setting out the grounds of appeal, opponent 1 filed five documents, including document D39 (see below for numbering).

VI. With the statement setting out the grounds of appeal, opponent 2 filed two documents and accompanying annexes.

VII. With the reply to the appeals, the patent proprietor filed sets of claims of a main request and auxiliary requests 1 to 15. The main request is identical to the request held allowable by the opposition division.

VIII. With letters dated 17 August 2023 and 14 February 2025, opponent 2 made further submissions.

IX. With letters dated 21 January 2025 and 6 February 2025 the patent proprietor made further submissions.

X. Opponent 3 did not make any substantive submissions in the appeal proceedings.

XI. With letter dated 22 January 2025, opponent 1 withdrew its appeal. Opponent 2 is therefore the sole remaining appellant. Opponents 1 and 3 are parties as of right to the appeal proceedings. The patent proprietor is respondent to the appeal.

XII. The board appointed oral proceedings and in two communications pursuant to Article 15(1) RPBA informed the parties of its preliminary view on some of the issues in the appeal.

XIII. Oral proceedings took place in the presence of the appellant and the respondent. Opponents 1 and 3 were not present, as announced beforehand. At the end of the oral proceedings, the Chair announced the board's decision.

XIV. Claim 1 of the **main request** reads as follows.

"1. A compound represented by the following structural formula

[formula of eliglustat]

or a pharmaceutically acceptable salt thereof, for use in a method of treating a subject with Gaucher disease, the method comprising:

testing the subject to determine whether the subject is a poor, intermediate or extensive/ultra rapid P450 metabolizer, wherein

the subject is assessed as being a poor, intermediate or extensive/ultra rapid P450 metabolizer through genotyping, wherein a poor P450 metabolizer carries two mutant alleles of the CYP2D6 gene which result in complete loss of enzyme activity, an intermediate P450 metabolizer possesses one reduced activity allele and one null allele of the CYP2D6 gene, an extensive P450 metabolizer possesses at least one and no more than two normal functional alleles of the CYP2D6 gene, and an ultra rapid P450 metabolizer carries multiple copies of functional alleles of the CYP2D6 gene and produces excess enzymatic activity; and

administering to the subject an adjusted effective amount of the compound if the subject is an intermediate or extensive/ultra rapid P450 metabolizer and administering to the subject an effective amount of the compound if the subject is a poor P450 metabolizer, wherein said effective amount is a daily dose of from 25 milligrams to 300 milligrams, and wherein said adjusted effective amount is greater than said effective amount."

Claim 1 of auxiliary requests 1 to 15 differs from the main request and from each other in a number of features. However, what is relevant for the purposes of

this decision is the definition of the "effective amount".
Claim 1 of **auxiliary request 1** defines that the "effective amount is a daily dose of from 25 miligrams to 300 mg daily".
In claim 1 of **auxiliary requests 2 and 3** the range is 25 to 150 mg daily.
In claim 1 of **auxiliary requests 4 and 5** the range is 50 to 300 mg daily.
In claim 1 of **auxiliary requests 6 and 7** the range is 50 to 150 mg daily.
In claim 1 of **auxiliary requests 8 to 15** the effective amount is 100 mg daily.
The "adjusted effective amount" is defined in all requests as "greater than said effective amount".

XV. The following documents are referred to in this decision:

D1: Peterschmitt, JP *et al.*, Molecular Genetics and Metabolism 96, Abstract 102, 2009, pages S12-S47

D9: Belle, DJ and Singh, H, American Family Physician 77(11), 2008, pages 1153-1560

D39: Prescribing information "CERDELGA™ (eliglustat) capsules, for oral use Initial U.S. Approval 2014", dated 19 August 2014, 24 pages

XVI. The appellant's arguments, where relevant to this decision, may be summarised as follows:

Main request
Disclosure of the invention (Article 83 EPC)

Claim interpretation

The only limitation defined in the claim as regards the dose for the patients that are intermediate or extensive/ultra rapid metabolisers was that it should be greater than the dose for those that are poor metabolisers (PM).

The case law of the boards of appeal

The requirements for sufficiency of disclosure for a claim defining a dosage regimen differed from those for a claim defining a new medical indication (see T 609/02, Reasons 8, referring to the technical contribution to the state of the art). Specifically, the requirement for a classical second medical use of a compound was that the therapeutic effect of the compound was credible. In the case at hand, this was already known, because document D1 disclosed eliglustat for the treatment of Gaucher disease. Therefore, the application as filed had to disclose additional information relating to the technical contribution to the state of the art, in accordance with decision T 609/02. The appropriate standard was set out in decision T 1592/12. It was not a low hurdle, such as not incredible, or not implausible. In fact, decision G 2/21 referred to the requirement of "proof of the claimed therapeutic effect" (see Reasons 77; see also decision T 294/20). The case underlying decision T 950/13, cited by the respondent, differed from the case at hand.

The disclosure in the patent

The patent lacked any disclosure in respect of (i) a link between a patient's genotype and their metaboliser status in patients with Gaucher disease; (ii) a link between the metaboliser status and the clinical relevance of adjusting the dose of eliglustat; (iii) a link between each of the two patient groups, i.e. PM patients and non-PM patients, and the dose to be administered.

Example 9 could not substantiate sufficiency of disclosure because, despite showing the therapeutic effect of eliglustat on patients with Gaucher disease, it did so without any information on their metaboliser status; Example 13 related to other embodiments in the application, namely drug-drug interactions; Example 13 did not allow conclusions to be drawn with respect to Gaucher disease for the additional reason that it involved only healthy subjects (see in this context document D13); as regards the doses, Example 13 did not explain the impact of the inhibition experiment on the metabolism, i.e. to what extent the reduction in metabolism correlated to patient metaboliser status, i.e. whether a PM or other; further, doses for PM patients could not be extrapolated from this example.

The target plasma levels for eliglustat mentioned in paragraph [0059] of the patent were not recited in the claim or measured in the examples. However, this meant that the target plasma levels were relevant, rather than the administered amounts of eliglustat. Furthermore, determining the appropriate doses based on the plasma levels amounted to an undue burden.

Claim 1 did not specify the dose range for non-PM patients. There was no information on how much "*greater*" the "*adjusted effective amount*" should be. Both the "*effective amount*" for PM patients and the "*adjusted effective amount*" for non-PM patients could be in the same range of 25-300 mg daily.

Conclusions

In view of the claim construction and the disclosure in the patent, the doses defined in claim 1 were not sufficiently disclosed.

Auxiliary requests 1 to 15
Disclosure of the invention (Article 83 EPC)

The patent contained no evidence that 100 mg daily was the dose to be administered to a PM patient. There was no evidence confirming the therapeutic window for eliglustat. The examples in the patent did not show the administration of 100 mg daily to a PM patient with Gaucher disease. Paragraph [0061] of the patent indicated both 100 mg daily and 200 mg daily as suitable doses for PM patients with Gaucher disease.

Thus, the same conclusion as that set out with respect to the main request also applied to the auxiliary requests.

XVII. The respondent's arguments, where relevant to this decision, may be summarised as follows:

Main request
Disclosure of the invention (Article 83 EPC)

Claim interpretation

The claim defined a dose in the range of 25 to 300 mg daily for PM patients and a dose greater than the dose for PM patients for non-PM patients. The appropriate dose for a given patient depended on factors such as patient's weight and age (see paragraph [0059] of the patent). In practice, the dose for a given patient was first determined on the basis of the patient being a PM; in the case of a non-PM patient, a greater dose was to be administered. The daily dose for the non-PM patient group could also fall within the range 25 to 300 mg. The claim did not exclude a dose of 200 mg daily for these patients, provided that the dose for a PM patient was less than 200 mg daily. It also did not exclude a dose of 400 mg daily for a non-PM patient.

The case law of the boards of appeal

The disclosure of the invention was sufficient if the technical effect recited in the claim was credible. Decision T 609/02 recognised that the patent system should take into account the difficulties in obtaining regulatory market authorisation by allowing early filing. Accordingly, the hurdle for sufficiency of disclosure was low.

Absolute proof of a given technical effect was not required and not supported by the case law. In decision T 950/13, the board accepted sufficiency of disclosure on the basis of a "plausible technical concept", provided there were no substantiated doubts. In other words, provided there was no *a priori* teaching that the

invention was implausible and provided there was "testable" evidence in the patent, rather than a mere verbal statement, then the information in the patent had a technical character and there was no lack of sufficient disclosure. Decision T 294/20 was in line with that established case law and did not support setting higher standards for sufficiency of disclosure.

Furthermore, requiring absolute proof would preclude dosage regimens from patent protection, since the necessary clinical trials were carried out at a stage when information was already in the public domain.

Decision T 609/02 recognised the need for a balance and decision G 2/21 did not change this standard. Decisions of the boards of appeal issued after decision G 2/21 confirmed this interpretation. It sufficed that the technical effect set out in the claim was credible. The requirements for sufficiency of disclosure for claims directed to therapeutic indications defining a dosage regimen were no different to the requirements set out in decision T 609/02. This was supported by decision T 2015/20 (see Reasons 2.6) and was consistent with decision G 2/08. The only question to be assessed was whether there was a treatment effect in the patient population defined in the claim. Only the technical effects recited in the claim were relevant for the assessment of sufficiency of disclosure and it would be inappropriate to read into the claim any technical effects not recited therein.

The disclosure in the patent

A therapeutic effect of eliglustat on Gaucher disease was made credible by Example 9 of the patent. The requirements for sufficiency of disclosure for claims

directed to therapeutic indications defining a dosage regimen were no different to the requirements for any other therapeutic indication. Furthermore, it was credible from the patent that different genotypes required different doses of eliglustat (Example 13). Therefore, the claimed invention was sufficiently disclosed.

In case more information was considered required for a sufficient disclosure, reference was made to the following observations:

(i) Example 13 of the patent showed a link between genotype and the need for dose adjustment: as regards a link between inhibition testing and metaboliser status, see also document D20; although healthy subjects were tested, the conclusions from the inhibition test also applied to patients with Gaucher disease, as there was no reason to believe that CYP2D6 levels would be altered in these patients (based on document D13, page 424, the skilled person would expect the opposite to be the case). Therefore, it was entirely plausible that by dosing the two patient groups differently, the dosage regimen was improved. Moreover, the skilled person knew of drugs for which dose adjustment in view of CYP2D6 metaboliser status was appropriate. In view of this knowledge, it was not implausible for the skilled person that a dose adjustment was appropriate.

(ii) Example 9 showed efficacy of doses of 100 mg and 200 mg eliglustat daily for the treatment of Gaucher disease;

(iii) the patent was to be read as a whole; further guidance on the selection of an appropriate dose was provided in paragraph [0059] of the patent, which

taught that the appropriate dose depended on factors such as the patient's weight and age - the range in the claim reflected the teaching in paragraph [0059] and provided for an appropriate dose for different subjects;

(iv) still further guidance was provided by the eliglustat target concentration in serum - 5 ng/l to 100 ng/l (see paragraph [0059] of the patent); determining the level of drugs in plasma was routine and did not involve an undue burden.

Furthermore, the regulatory market authorisation for eliglustat at 100 mg and 200 mg daily was proof that the dose was appropriate.

The principle to be applied was whether the effect recited in the claims was achievable across the dose range of 25 to 300 mg daily. Given that the compound was approved for the treatment of Gaucher disease at a dose of 100 mg daily for adults, it was credible that a dose of 25 mg would be appropriate for example for children. There were no facts on file that would cast doubt on this. Likewise, it was credible that a dose of 300 mg daily was therapeutically effective.

Auxiliary requests 1 to 15
Disclosure of the invention (Article 83 EPC)

No arguments applying specifically to auxiliary requests 1 to 9 and 11 to 15 were submitted.

As regards auxiliary request 10, claim 1 specified an effective dose of 100 mg daily, which was the approved dose. Post-published data confirmed the suitability of this dose (see document D39). This was also the dose

that was taught in the patent when read as a whole. Despite the statement in paragraph [0061] of the patent, which indicated both 100 mg daily and 200 mg daily as the dose for PM patients, a daily dose of 100 mg was the teaching of the patent as a whole. Example 9, which described the administration of 100 mg daily or 200 mg daily, was consistent with the dose in claim 1. There was no reason for the skilled person to believe this dose was implausible.

Paragraph [0059] of the patent provided a reasonable range for the target plasma concentration of eliglustat (5 to 100 ng/ml), with the upper end of the range being 20-fold higher than the lower end of the range. The target plasma concentration of 5 ng/ml was in the order of magnitude of IC50 for eliglustat.

Requests of the parties

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

Opponent 1 requested that the decision under appeal be set aside and the patent be revoked in its entirety.

The respondent requested that the appeal be dismissed and the patent be maintained in amended form on the basis of the main request held allowable by the opposition division, the claims of which were re-filed in appeal (main request); alternatively, that the patent be maintained on the basis of one of the sets of claims of auxiliary requests 1 to 15. Further, it requested that the documents filed in the appeal proceedings by opponents 1 and 2 not be admitted into the appeal proceedings.

Reasons for the Decision

Admittance into the appeal proceedings of documents filed in appeal proceedings by opponents 1 and 2

1. The board did not need to take a decision on the admittance or otherwise of any of the documents whose admittance was disputed by the respondent because they were not relevant to the final decision taken.

Main request (held allowable by the opposition division)
Disclosure of the invention (Article 83 EPC) - Claim 1

2. Claim 1 is drafted in the form of a purpose-limited product claim, pursuant to Article 54(5) EPC, and is directed to eliglustat for use in the treatment of Gaucher disease. The claim defines a step of genotyping the patient for alleles of the CYP2D6 gene, to correlate this genotype with the patient's P450 metaboliser status, and a step of administering eliglustat to the patient. It defines two patient groups: a group consisting of poor metabolisers (PM) and a group consisting of intermediate and extensive/ ultra rapid metabolisers, i.e. all patients other than poor metabolisers. The dose to be administered to the second group is defined by reference to the dose to be administered to the first group, i.e. poor metabolisers, which itself is defined by a range of 25 mg to 300 mg daily.

3. It was common ground that the claim defines two groups of patients, defined by their metaboliser status. There

was dispute as to whether these groups are dosed differently.

4. In line with the case law of the boards of appeal, where a therapeutic application of a compound is claimed, attaining the claimed therapeutic effect is a functional technical feature of the claim and the requirements of Article 83 EPC are only met if the patent discloses the suitability of the compound for the claimed therapeutic application, unless this was already known to the skilled person at the priority date (see decision T 609/02, Reasons 9). "Suitability" of the compound for the therapeutic application requires that from the patent it is credible that the claimed therapeutic effects are achieved (see decision G 2/21, OJ 2023, A85, Reasons 77).

5. The key issue in this appeal was which of the features characterising the claimed therapeutic application had to be disclosed in the patent. In other words, whether the information required in line with decision T 609/02 concerned only the suitability of eliglustat for treating Gaucher disease or whether it concerned also the suitability of each dose in the claim for the respective patient group.

6. In the present case, the claimed therapeutic application is the treatment of Gaucher disease with eliglustat, in two patient groups as defined in the claim, at the respective dose of eliglustat. In the board's view, when applying the principles set out in decision T 609/02 to the present claim 1, what must be disclosed in the application is therefore the suitability of eliglustat for treating Gaucher disease at these different doses for the different patient

groups. It does not suffice to merely disclose the suitability of eliglustat for treating Gaucher disease.

7. In the board's view, classifying patients into two groups without guidance on how the dose differs between them would be an incomplete teaching which would not provide the skilled person with sufficient information to put the invention into practice. Hence, what remains to be assessed is whether the application provided such guidance on the different doses for the two patient groups defined in the claim.

8. The respondent argued, referring to decision T 609/02, that it was well established in the case law of the boards of appeal that sufficiency of disclosure only required some information linking the claimed subject-matter to a relevant metabolic pathway, and that decision T 950/13 provided an example where this requirement was met despite limited experimental evidence in the patent.

9. As set out above, the board derives from decision T 609/02 that sufficiency of disclosure requires showing the suitability of the dose for the respective patient group (see point 6.). This is not in contradiction with decision T 950/13, which did not deal with the question of the features in the claim that require a disclosure in the application, but instead dealt with the level or quality of information required, or in other words with the question of whether a technical concept may be accepted for demonstrating the suitability in the absence of any experimental data. The same applies to decision T 321/15, which was also cited by the respondent as an example where a therapeutic effect was considered credible despite the absence of experimental data.

10. The appellant further referred to decisions T 2015/20 and T 108/21 to demonstrate that a low threshold applies for assessing sufficiency of disclosure of claims directed to medical uses. However, also in these decisions, the board did not address the issue at hand, which is that the dose specified for each of the two patient groups identified in the claim is a technical feature of the claim.

10.1 In decision T 2015/20, the board considered the question of sufficiency of disclosure of a claim directed to a compound for use in the treatment of asthma at a dose of 400 µg by inhalation, where the application provided information only for the effect of the compound in a different disease, i.e. chronic obstructive pulmonary disease (COPD). At issue was therefore whether the suitability of the compound for a different disease was credible. However, at issue in the present case is the suitability of a specific dose range for a specific patient group.

10.2 Nevertheless, the respondent pointed out that according to decision T 2015/20, serious doubts were required to substantiate an objection of a lack of sufficiency of disclosure and that in the absence of support for such serious doubts, and in view of the fact that the claimed invention did not go against a prevailing technical opinion, the requirement of sufficiency of disclosure was met.

10.3 This is not the view of the present board. Sufficiency of disclosure requires foremost that the application disclose the suitability of the compound for the claimed therapeutic application, in line with decision T 609/02, which states that "*unless this is already*

known to the skilled person at the priority date, the application must disclose the suitability of the product ... for the claimed therapeutic application" (Reasons 9). When this is not clearly the case, the opponent may simply rely on arguments to challenge the sufficiency of disclosure of the patent.

10.4 The respondent further referred to T 108/21, in support of the argument that sufficiency of disclosure does not require experimental data obtained with the dose specified in the claim. It related to a case where the only data was obtained in an experimental model of the medical indication in the claim, with a different dose administered from that defined in the claim.

10.5 The board considers that decision T 108/21 confirms the case law of the boards of appeal as represented for example by decision T 801/06, according to which a "*therapeutic effect may be proven by any kind of data as long as they clearly and unambiguously reflect the therapeutic effect*" (see Reasons 28; see also decision T609/02, Reasons 9). As regards the relevance to the present case, the board notes that in the case underlying decision T 108/21, the board found that in order to comply with the requirements of Article 83 EPC "*the application as filed must disclose the suitability of fingolimod (salt) at an oral daily dose of 0.5 mg for the claimed therapeutic application*" (see Reasons 5.3). Based on the nature of experiments disclosed in the patent, and in view of the animal model used therein, the board then concluded that the findings relating to the dose in the animal model translated into the suitability of the claimed dosage regimen for the therapeutic application claimed (see Reasons 5.13). Therefore, in decision T 108/21 the board only held that the invention as claimed was

sufficiently disclosed after it fully assessed the suitability of the compound in the dose defined in the claim. The board in the present case concludes that decision T 108/21 does not support the respondent's arguments according to which the application is only required to show the suitability of the compound for treating the disease. The board notes that indeed the respondent cited this decision to address the requirements regarding the nature of the experimental data in the patent rather than the claim features for which disclosure is required.

11. A requirement that the application disclose the suitability of the compound in the claimed dose, as set by the board in decision T 108/21 (see Reasons 5.3), was also set by the board in decision T 1592/12. In that decision, the board considered a claim which related to the use of an antibody (Herceptin®) for treating patients with breast cancer by administering an initial dose of 8 mg/kg followed by maintenance doses of 6 mg/kg every three weeks. The board in that decision expressly rejected the argument put forward by the appellant in that case, which is analogous to the respondent's argument in the present case, that disclosing the suitability of the antibody for treating the type of breast cancer defined in the claim sufficed to comply with the requirements of sufficiency of disclosure (see Reasons 18). The reason for this was that the technical contribution was not the provision of the antibody Herceptin® for treating patients with breast cancer but rather the claimed dosage regimen (see Reasons 19). Hence, while the respondent in the present case argued that ultimately sufficiency of disclosure was denied due to the serious doubts raised, this argument does not change the requirements set by the board in T 1592/12, i.e. that the suitability of

the dosage regimen must be disclosed in the application.

12. Decision T 391/18 was cited by the respondent for providing yet a further example of "initial plausibility" for a claim defining once-daily administration of a compound. The board considered a claim directed to a combination therapy for treating HIV infection by daily administration of compound TMC278 and a nucleoside reverse transcriptase inhibitor or nucleotide reverse transcriptase inhibitor. A dose was not defined in the claim. According to the respondent, sufficiency of disclosure was acknowledged despite the absence of any experimental data relating to combination therapy and the unpredictability of drug-drug interactions.

12.1 The board in T 391/18 considered whether the application disclosed the suitability of TMC278 for treating HIV by once-daily administration and concluded in the affirmative (see Reasons 2.2, third and last paragraphs). As regards the second compound in the combination therapy, the board concluded that several compounds according to the definition in the claim had already been approved for once-daily administration in the treatment of HIV (see Reasons 2.3). The issue pointed out by the respondent is therefore that of the suitability of a combination starting from the suitability of each compound individually. However, of relevance for the present case is the suitability of each dose for each specific patient group in a therapeutic application. Thus, the present board concludes that there is no divergence between the present decision and decision T 391/18 as regards the requirements for the application to disclose the suitability of the compound in the dose claimed.

The disclosure in the patent

13. In addition to arguing that the case law did not support a requirement for showing the suitability of the dose for the patient group, the respondent argued that the patent shows a link between different patient genotypes, i.e. different patient groups, and a differentiated dosage. The board is of the view that this link is credible from the information provided in Example 13 of the patent, and further in light of common general knowledge. However, information is lacking as regards the dose to be given to each of the two patient groups. It is recalled that claim 1 defines that the dose for a patient assessed to be non-PM is greater than the dose for a patient assessed as PM. However, there is no information making credible the suitability of a dose in the range of 25-300 mg for PM patients and there is no information on the dose range for non-PM patients, or at least on how much greater that dose should be.

14. The patent contains information about the therapeutic effect of eliglustat in patients with Gaucher disease at a dose of 100 mg or 200 mg daily (Example 9). The patients are not, however, characterised as to their metaboliser status or CYP2D6 genotype. The patent further discloses that a CYP2D6 inhibitor interfered with eliglustat metabolism (Example 13), from which it is inferred in the patent that CYP2D6 plays a significant role in the metabolism of eliglustat.

15. The patent does not disclose how the suitable dose is affected by the metaboliser status. Moreover, the patent does not disclose the suitability of the dose range of 25-300 mg daily for poor metabolisers.

Likewise, the patent does not disclose the suitability of the range of 25-300 mg daily, or any other dose range, for non-PM patients. The suitability of the range 25 to 300mg cannot be extrapolated from Example 9, where the patients are administered 100mg or 200mg daily, for either of the patient groups defined in claim 1. There is no information in the patent on how the dose for non-PM patients differs from that known from the prior art, as disclosed in document D1, which discloses the same study as Example 9 of the patent. The patent does not disclose to what extent the dose should be higher than that set out for PM patients. It does not disclose whether, for example, it should be double, or triple, or 10% higher. As such, the skilled person is left to determine the impact the metaboliser status has on the appropriate dose: whether the doses known from the prior art document D1, i.e. either 100 mg or 200 mg daily, are suitable for PM patients, and whether a dose of either 100 mg or 200 mg is also suitable for non-PM patients.

16. The respondent argued that the contribution of the patent to the art resides in the appreciation of the relevance of CYP2D6 for eliglustat metabolism and in the plasma target concentration for eliglustat, in paragraph [0059]. For the reasons given above, the board considers that the skilled person is not provided with information on the dose suitable for each patient group. The respondent's argument that Example 9 supports the suitability of both doses for the treatment of Gaucher disease is not relevant to claim 1, which requires that the suitability of each dose range in the claim be shown for the corresponding patient group. Furthermore, it is apparent from Example 9 that both doses were efficacious for the participants of the study. It is known that the

frequency of a poor CYP2D6 metaboliser phenotype in the population is between 1% and 10%, depending on ethnicity (see Table 2 of document D9). Therefore, the larger part of the population is non-PM. It cannot be assumed that the patients in the study who were administered the dose of 100 mg daily were all PM. Conversely, from Example 9 it cannot be concluded that the lower dose of 100 mg daily was not efficacious for non-PM patients. The patent, however, does not provide any information on the dose that is suitable for the non-PM patient group.

17. In summary, the board has come to the conclusion that the invention defined in claim 1 is not sufficiently disclosed.

Auxiliary request 10
Disclosure of the invention (Article 83 EPC) - Claim 1

18. The respondent referred to paragraph [0061] of the patent, where it is stated that "*An effective amount for poor P450 metabolizers is (whether as a monotherapy or as a co-therapy) commonly between 100-200 milligrams per day, for example 100 or 200 milligrams, as a once daily dose or twice daily dose.*" However, this paragraph cannot be read in isolation. In the board's view, this statement in the patent contradicts Example 9, which discloses that doses of both 100 mg daily and 200 mg daily are efficacious for all participants in the study. The board concludes that paragraph [0061] does not provide the skilled person with the teaching that the suitable dose for PM patients is 100 mg daily.

19. The respondent referred to the FDA label for Cerdelga®, filed as document D39, as evidence that PM patients are administered 100 mg daily and non-PM patients 200 mg daily. In the board's view, this document contains an entirely new teaching. It cannot be seen as merely confirming the teaching in the patent. This is because the patent does not contain information showing a link between a given dose range of eliglustat and one of the two patient groups.

20. The above notwithstanding, the deficiencies discussed above as regards the suitable dose for non-PM patients remain for claim 1 of this request.

Auxiliary requests 1 to 9 and 11 to 15
Disclosure of the invention (Article 83 EPC) - Claim 1

21. The key issue for the finding of insufficient disclosure with respect to the main request was a lack of information concerning a link between each patient group and a dose range, in particular concerning the dose to be administered to non-PM patients, a dose out of an undefined range. This missing information also applies to the ranges in claim 1 of auxiliary requests 1 to 7.

22. The reasoning given for auxiliary request 10 also applies to auxiliary requests 8, 9 and 11 to 15, all of which define the effective amount and adjusted effective amount in the same way as auxiliary request 10.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairwoman:

I. Aperribay M. Pregetter

Decision electronically authenticated