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Datasheet for the decision of 27 February 2014

Case Number: T 0686/10 - 3.3.02

Application Number: 95939858.7

Publication Number: 804183

IPC: A61K31/195, A61K31/66, A61K31/675

Language of the proceedings: EN

Title of invention:
USE OF CREATINE OR CREATINE ANALOGS FOR THE TREATMENT OF HUNTINGTON'S DISEASE, PARKINSON'S DISEASE AND AMYOTROPHIC LATERAL SCLEROSIS

Patent Proprietors:
Avicena Group, Inc.
THE GENERAL HOSPITAL CORPORATION

Opponent:
Numico Research B.V.

Headword:
Use of creatine and cyclocreatine for the treatment of Huntington's disease and Parkinson's disease/ AVICENA

Relevant legal provisions:
EPC Art. 123, 83, 54(2), 111(1)

Keyword:
New main request at appeal proceedings
Remittal

Decisions cited:

Catchword:

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Case Number: T 0686/10 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 27 February 2014

Appellant-patentees: (Patent Proprietor 1)	Avicena Group, Inc. Building 200, Suite 2200, One Kendall Square Cambridge, MA 02139 (US)
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Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 19 January 2010 concerning maintenance of the European Patent No. 804183 in amended form.**

Composition of the Board:

Chairman: U. Oswald
Members: M. C. Ortega Plaza
B. Müller

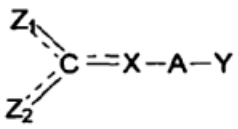
Summary of Facts and Submissions

I. European patent No. 0 804 183, based on European patent application No. 95939858.7, which was filed as an international patent application published as WO 96/14063, was granted with five claims.

Claim 1 as granted reads as follows:

Claims

1. Use of a creatine compound of the general formula:



and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of:

- CO_2H, -NHOH, $-NO_2$, - SO_3H, $-C(=O)NHSO_2J$ and
- $P(=O)(OH)(OJ)$, wherein J is selected from the group consisting of: hydrogen, C_1-C_6 straight chain alkyl, C_3-C_6 branched alkyl, C_2-C_6 alkenyl, C_3-C_6 branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, and C_2-C_5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C_1-C_6 straight alkyl, C_2-C_6 straight alkenyl, C_1-C_6 straight alkoyl, C_3-C_6 branched alkyl, C_3-C_6 branched alkenyl, and C_4-C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
2) an aryl group selected from the group consisting of: a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: $-CH_2L$ and $-COCH_2L$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and
3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_1-C_4 alkoyl, C_3-C_4 branched alkyl, C_3-C_4 branched alkenyl, and C_4 branched alkoyl;

c) X is selected from the group consisting of NR_1, CHR_1, CR_1, O and S, wherein R_1 is selected from the group consisting of:

1) hydrogen;
2) K where K is selected from the group consisting of: C_1-C_6 straight alkyl, C_2-C_6 straight alkenyl, C_1-C_6 straight alkoyl, C_3-C_6 branched alkyl, C_3-C_6 branched alkenyl, and C_4-C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
3) an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: $-CH_2L$ and $-COCH_2L$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
4) a C_5-C_9 a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;
5) a C_5-C_9 a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and
6) a C_5-C_9 a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z_1 and Z_2 are chosen independently from the group consisting of: =O, $-NHR_2$, $-CH_2R_2$, $-NR_2OH$; wherein Z_1 and Z_2 may not both be =O and wherein R_2 is selected from the group consisting of:

1) hydrogen;
2) K, where K is selected from the group consisting of: C_1-C_6 straight alkyl; C_2-C_6 straight alkenyl, C_1-C_6 straight alkoyl, C_3-C_6 branched alkyl, C_3-C_6 branched alkenyl, and C_4-C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
3) an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: $-CH_2L$ and $-COCH_2L$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;
4) a C_4-C_8 a-amino-carboxylic acid attached via the w-carbon;
5) B, wherein B is selected from the group consisting of: $-CO_2H$, - NHOH, $-SO_3H$, $-NO_2$, OP(=O)(OH)(OJ) and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C_1-C_6 straight alkyl, C_3-C_6 branched alkyl, C_2-C_6 alkenyl, C_3-C_6 branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: C_1-C_2 alkyl, C_2 alkenyl, and C_1-C_2 alkoyl;
6) -D-E, wherein D is selected from the group consisting of: C_1-C_3 straight alkyl, C_3 branched alkyl, C_2-C_3 straight alkenyl, C_3 branched alkenyl, C_1-C_3 straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: $-(PO_3)_nNMP$, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-[P(=O)(OCH_3)(O)]_m$-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-[P(=O)(OH)(CH_2)]_m$-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and $-CO_2G$, where G is independently selected from the group consisting of: C_1-C_6 straight alkyl, C_2-C_6 straight alkenyl, C_1-C_6 straight alkoyl, C_3-C_6 branched alkyl, C_3-C_6 branched alkenyl, C_4-C_6 branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and
7) -E, wherein E is selected from the group consisting of: $-(PO_3)_nNMP$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-[P(=O)(OCH_3)(O)]_m$-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-[P(=O)(OH)(CH_2)]_m$-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chose independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and $-CO_2G$, where G is independently selected from the group consisting of: C_1-C_6 straight alkyl, C_2-C_6 straight alkenyl, C_1-C_6 straight alkoyl, C_3-C_6 branched alkyl, C_3-C_6 branched alkenyl, C_4-C_6 branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;
f) if two R_2 groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and
g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of $-NHR_2$, $-CH_2R_2$ and $-NR_2OH$, then R_1 may be connected by a single or double bond to the carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members;

in the manufacture of a medicament for the treatment of, or preventing the occurrence of, or for the treatment of symptoms associated with Huntington's disease, Parkinson's disease or amyotrophic lateral sclerosis.

Claim 2 as granted reads as follows:

"2. Use as claimed in claim 1 of a compound selected from creatine and cyclocreatine".

II. Opposition was filed and revocation of the patent in its entirety was requested, in particular pursuant to Article 100(a) (lack of novelty and lack of inventive step) and 100(b) EPC (lack of sufficiency of disclosure).

III. The following documents *inter alia* were cited in the proceedings before the opposition division and the board of appeal:

D2 WO 94/17794
D6 WO 92/14697

IV. The present appeal lies from an interlocutory decision of the opposition division maintaining the patent in amended form on the basis of auxiliary request 4 filed with the letter of 17 July 2009 (Articles 101(3)(a) and 106(2) EPC).

V. The opposition division considered that the opposition was admissible. Rejecting the patentees' objections, the opposition division held that the opposition fulfilled the requirements of Rule 55(c) EPC 1973, since at least the ground of opposition under Article 100(b) EPC was sufficiently substantiated. The opposition also met the other requirements of Rule 55 EPC 1973 as well as those of Articles 99(1) and 100 and of Rule 1(1) EPC 1973.

Additionally, the opposition division considered that the main request (set of claims as granted) failed on grounds pursuant to Article 100(b) EPC. In particular, the technical effect of the claimed compounds was attributed to their resemblance to creatine, and creatine could be considered as a representative compound for the "creatine analogues" in tables 1 and 2 of the patent in suit. However, claim 1 encompassed compounds bearing such considerable structural modifications and differences when compared to creatine that they did not have a minimum structural commonality

with it (as an example, the compound 4-methyl pentanoic acid was mentioned).

As regards auxiliary request 1, filed with the letter dated 24 January 2008, the opposition division considered that it failed for reasons analogous to those given for the main request.

As regards auxiliary requests 2 and 3, filed with the letter dated 24 January 2008, the opposition division considered that they met the requirements of Article 123(2) EPC. As regards Article 100(b) EPC, the opposition division considered that the Markush formula and the accompanying definitions in claim 1 were such that they did not encompass compounds in which Z_1 or Z_2 were =NR (or =NH), and thus creatine and cyclocreatine were not encompassed. The opposition division considered that these discrepancies resulted in serious problems under Article 100(b) EPC for auxiliary request 2. Moreover, according to the opposition division, auxiliary request 3 failed for reasons analogous to those relating to the previous request.

As regards auxiliary request 4, filed with the letter of 17 July 2009, the opposition division was of the opinion that the introduced amendments were caused by grounds of opposition and that the amended claims met the requirements of Article 123(2) and (3) EPC. In the opposition division's view, the claimed subject-matter furthermore met the requirements of novelty since document D2 disclosed compositions of creatine also containing a sugar. In addition, the opposition division considered that document D2 did not anticipate the subject-matter claimed since it "constitute(d) a non-enabling disclosure".

In relation to inventive step of the subject-matter claimed in auxiliary request 4, the opposition division was of the opinion that document D2 did not provide any reason to leave away the sugar or suggest that there would be beneficial effects. In the opposition division's view, document D6 was less relevant.

Additionally, the opposition division was also of the opinion that auxiliary request 4 met the requirements of sufficiency of disclosure.

Finally, the opposition division refused the opponent's request for apportionment of costs (Article 104 EPC). The opposition division considered that the patentees had withdrawn their request for oral proceedings shortly before the date of oral proceedings; however, such a withdrawal did not amount to culpable conduct and could not be a factor in assessing whether reasons of equity existed under Article 104(1) EPC. The opposition division further considered that the opponent had requested oral proceedings on an auxiliary basis for the eventuality that the patent was not revoked on the basis of its written submissions. Moreover, in the opposition division's view, in the light of the preliminary opinion it had expressed in its communication sent as an annex to the summons, the opponent could not have expected that its request for revocation would prevail. Therefore, the opposition division was not convinced that if the opponent had known earlier that the patentees would not be attending the oral proceedings, it would also have decided not to attend them.

VI. The opponent (appellant-opponent) lodged an appeal against said decision and filed grounds thereto.

VII. The patent proprietors (appellant-patentees) lodged an appeal against said decision and filed grounds thereto.

VIII. With its grounds of appeal dated 21 May 2010 the appellant-opponent requested that the patent be revoked and that the opposition division's decision refusing apportionment of costs be overturned.

Additionally, the appellant-opponent submitted that auxiliary request 4 before the opposition division did not comply with the requirements of Article 123(2) and (3) EPC. Moreover, the subject-matter of claim 1 lacked novelty vis-à-vis document D2 and lacked inventive step in view of documents D2 and D6.

IX. With their grounds of appeal dated 25 May 2010 the appellant-patentees filed seven auxiliary requests. The appellant-patentees stated that auxiliary requests 1 to 3 corresponded to auxiliary requests 1 to 3 before the opposition division, that auxiliary request 4 was a new auxiliary request, and that auxiliary requests 5 to 7 were filed as a response to a possible opponent's appeal.

X. With a letter dated 14 October 2010 the appellant-opponent filed a response to the appellant-patentees' grounds of appeal.

XI. With a letter dated 28 October 2010 the appellant-patentees filed a response to the appellant-opponent's submissions and grounds of appeal. With said letter they filed two further auxiliary requests, auxiliary requests 8 and 9.

XII. On 9 December 2013 the board sent a communication pursuant to Article 15(1) RPBA as an annex to the summons to oral proceedings.

In said communication the board pointed out that auxiliary request 1 filed with the grounds of appeal was not identical to auxiliary request 1 before the opposition division. In particular, in claim 1 the definition of A as C_2-C_5 alkenyl had been deleted and the definition of R_2 (which appears in connection with the residues Z_1 and Z_2, option 5)), had been modified by replacing $-SO_3H$ by $-SO_2H$. Analogous comments applied to auxiliary requests 2 and 3. Therefore, the board requested the appellant-patentees to identify each and every difference between the auxiliary requests filed in appeal proceedings and the claims as granted.

Moreover, in said communication, the board expressed the opinion that the opposition division had correctly found the opposition admissible and gave reasons therefor.

In said communication the board also mentioned that the opposition division had assessed the grounds pursuant to Article 100(b) and Article 100(a) EPC (novelty and inventive step) and decided thereon in the decision under appeal. Consequently, all these grounds of opposition were within the framework of the present appeal.

The board also expressed the preliminary opinion that the opposition division's decision to refuse the opponent's request for apportionment of costs under Article 104 EPC was correct.

XIII. The appellant-patentees did not file any substantive reply to the board's communication with their letter dated 27 January 2014.

XIV. The appellant-opponent filed a letter dated 10 February 2014 in which it stated that it maintained its request that the patent be revoked in its entirety.

XV. Oral proceedings took place on 27 February 2014.

XVI. At the oral proceedings before the board the appellant-patentees withdrew their request that the opposition be found inadmissible. Moreover, the appellant-patentees withdrew the main request before the opposition division (set of claims as granted), and the auxiliary requests 1 to 7 filed with the grounds of appeal. However, they maintained auxiliary requests 8 and 9 filed on 28 October 2010, which became their main request and auxiliary request, respectively.

XVII. **The appellant-patentees' main request relates to the set of claims (four claims) filed as auxiliary request 8 on 28 October 2010.** Claim 1 of the main request reads as follows:

"1. Use of a creatine compound and pharmaceutically acceptable salts thereof, wherein the creatine is selected from creatine and cyclocreatine in the manufacture of a medicament for the treatment of, or preventing the occurrence of Huntington's disease or Parkinson's disease".

XVIII. The appellant-opponent's arguments, as far as relevant for the decision, may be summarised as follows.

(a) The opponent objected to claim 1 of the main request under Article 123(2) and (3) EPC. Neither creatine nor cyclocreatine was encompassed by the Markush formula and the corresponding definitions in claim 1 as granted. Therefore, claim 2 as granted had to be considered an independent claim. As a result, the mention in claim 1 of the main request of pharmaceutically acceptable salts contravened the requirements of Article 123(3) EPC. In relation to Article 123(2) EPC, the appellant-opponent mentioned that claim 13 as originally filed referred to the group consisting of creatine, creatine phosphate, cyclocreatine and cyclocreatine phosphate. Therefore, there had been a double selection in claim 1 of the main request concerning on the one hand the pharmaceutically acceptable salts of creatine and cyclocreatine and on the other hand the diseases to be treated.

The appellant-opponent further submitted that the appellant-patentees' explanations about analogies for interpreting the meaning to be given to the rests and residues in claim 1 as granted were difficult to follow and that they put an undue burden on the skilled person when reading the granted claims since there was no basis in the description of the patent in suit for taking such an approach.

The appellant-opponent did not raise any objections on grounds pursuant to Articles 100(b) (sufficiency of disclosure) and 100(a) EPC (novelty) to the subject-matter claimed in the new main request.

(b) As regards its request for overturning the opposition division's decision on apportionment of costs, the appellant-opponent submitted that the

patentees had informed the EPO and the opponent that they would not be attending the oral proceedings before the opposition division only in the afternoon of the day before the oral proceedings. The appellant-opponent argued that if the opponent had been informed earlier, it could have chosen not to attend the oral proceedings before the opposition division.

However, when asked by the board about its attendance at the oral proceedings before the opposition division, the opponent acknowledged that attending those oral proceedings had been useful for the defence of its interests.

XIX. The appellant-patentees' arguments, as far as relevant to the present decision, may be summarised as follows.

(a) It was self-evident for the skilled person, when reading claims 1 and 2 as granted and taking the granted claims as a whole, that the definitions given in claim 1 for some of the rests and residues presented some problems when combined with the depicted Markush formula. In particular, the definition of A in the rest -A-Y as being C_1-C_5 alkyl, C_2-C_5 alkenyl or C_2-C_5 alkynyl required, that a hydrogen atom had to be dropped in order that the residue -A be also linked to the residue -Y. The definition in option e) for R_1 and R_2 required that some of the definitions given for these residues also dropped a hydrogen atom. By analogy, the definitions of Z_1 and Z_2 being $-NHR_2$, together with the dotted line, would have been understood in the sense that a hydrogen atom had to be dropped and the delocalised double bond was present as $=NR_2$. Moreover, claim 1 as granted explicitly mentioned the use of a creatine compound and pharmaceutically acceptable salts thereof. Thus, it was not logical to exclude the

pharmaceutically acceptable salts of creatine and cyclocreatine. Therefore, the skilled person would understand that claim 2 as granted necessarily encompassed the pharmaceutically acceptable salts of creatine and cyclocreatine.

Creatine and cyclocreatine and their uses for the treatments now specified in claim 1 were disclosed as the most preferred (page 41, first paragraph of the application as filed) and they were also specifically illustrated in the examples, which concerned experiments with the models for Huntington's disease and Parkinson's disease. There had been no double selection since the paragraph at the top of page 41 specified both creatine and cyclocreatine together with the two diseases mentioned in claim 1. Moreover, creatine phosphate and cyclocreatine phosphate were the direct metabolites of the two active agents creatine and cyclocreatine. Correspondingly, the appellant-opponent's objections were artificially constructed and did not take into account that the application as filed had to be read by the skilled person. Therefore, the subject-matter claimed in claim 1 was directly and unambiguously disclosed in the application as filed.

Since the appellant-opponent had not raised any objections based on grounds pursuant to Articles 100(b) (sufficiency of disclosure) and 100(a) EPC (novelty) to the subject-matter claimed in the new main request, the appellant-patentees did not wish to submit any further comments in relation to these issues.

(b) The appellant-patentees submitted that although the patentees had not attended the oral proceedings before the opposition division, there was a reason for the opponent to attend them. In fact, very relevant aspects

of the objections against claim 1 as granted were discussed for the first time at those oral proceedings.

The fact that the patentees had chosen not to come to the oral proceedings before the opposition division was not an abuse of procedure but a question of money. The patentees' representative had informed the opposition division and the opponent that the patentees would not be attending the oral proceedings as soon as his clients had informed him that they did not give the authorisation to attend. With the same letter filed by fax the day before the oral proceedings before the opposition division the patentees had withdrawn their request for oral proceedings.

XX. After the discussion reflected in points XVIII(a) and XIX(a) above for the main request had taken place at the oral proceedings before the board, the parties were informed of the board's intention to remit the case to the department of first instance for further prosecution. The parties were then asked whether they wanted to make any observations in this respect.

The appellant-patentees first submitted that they had no objections against the remittal and thereafter made it clear that they were in favour of remittal to the department of first instance for the inventive step issue.

The appellant-opponent submitted that it objected to remittal to the department of first instance, since the only issue left in respect of the new main request was the assessment of inventive step. The appellant-opponent further submitted that its arguments in relation to the issue of inventive step were simple and thus they could be dealt with at the oral proceedings

before the board. Moreover, it recalled that the filing date of the application for which the patent in suit had been granted was 7 November 1995. Therefore, in the public interest, the case should be dealt with as soon as possible.

XXI. The appellant (patent proprietors) requested that the decision under appeal be set aside and the patent be maintained in amended form on the basis of the main request or auxiliary request filed as auxiliary requests 8 and 9, respectively, on 28 October 2010.

XXII. The appellant (opponent) requested that the decision under appeal be set aside and that the European patent No. 804183 be revoked. It further requested that the opposition division's decision to refuse apportionment of costs pursuant to Article 104 EPC be overturned.

Reasons for the Decision

1. The opposition division correctly considered that the opposition was admissible since it fulfilled the requirements of Rules 1(1) and 55 EPC 1973 and of Articles 99(1) and 100 EPC 1973.

More particularly, as to Rule 55(c) EPC 1973, a statement of the grounds of opposition was filed together with the notice of opposition. That statement set out the grounds on which the opposition was based (Articles 100(b) and 100(a) EPC) and also included facts, evidence and arguments presented in support of at least one of those grounds, i.e. the ground under Article 100(b) EPC. This suffices for the purpose of the admissibility of the opposition.

Additionally, the appellant-patentees no longer contest the admissibility of the opposition.

2. Both appeals are admissible.

3. *Main request*

3.1 Article 123(2) and (3) EPC

3.1.1 The board does not share the appellant-patentees' assessment of claim 1 as granted. While it may be quite common in patent jargon to employ the terms alkyl, alkenyl and alkynyl as representing alkylene, alkenylene and alkynylene residues in a particular generic formula, one cannot invoke this very particular situation as a generally accepted principle which would be always applicable by analogy for allowing the replacement of hydrogen atoms by links to other residues in any given generic formula. Additionally, if one considers, for the sake of argumentation, that the dot lines in the Markush formula in claim 1 as granted should be understood as a delocalised double bond, then the definition given in option e) of claim 1 as granted for R_1 and R_2 which reads: "if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members" would require, in order that cyclocreatine is encompassed by claim 1 as granted (i.e. after choosing X as NR_1, -A- as $-CH_2-$ and Y as CO_2H), not only that a hydrogen atom is dropped, but that either R_1 is dropped (and then it is the N atom of the rest NR_1, and not R_1 itself, which is linked to one R_2 for building a cycle) or one R_2 is dropped and the other R_2 is selected to be hydrogen (since both Z_1 and Z_2 have to be selected as $-NHR_2$). Similar problems arise when trying to identify

definitions in claim 1 as granted which could serve as valid options for creatine. Thus, the skilled person cannot conclude that creatine and cyclocreatine are encompassed by claim 1 as granted.

3.1.2 However, claim 2 as granted is formulated as concerning a use according to claim 1 as granted. Claim 1 is in Swiss-type form and relates to the use of "a creatine compound" and "pharmaceutically acceptable salts thereof" "in the manufacture of a medicament for the treatment of, or preventing the occurrence of, or for the treatment of symptoms associated with Huntington's disease, Parkinson's disease or amyotrophic lateral sclerosis".

The fact that a detailed study of claim 1 shows that the definitions of the rests and residues given in claim 1 as granted for the Markush formula depicted therein do not encompass creatine or cyclocreatine does not change the fact that claim 2 as granted specifically identifies creatine and cyclocreatine and includes a reference to claim 1 as granted. Therefore, in view of this reference to claim 1 as granted, from a technically meaningful reading of claim 2 as granted one can only conclude that claim 2 as granted includes the use of creatine, cyclocreatine and their pharmaceutically acceptable salts for the treatments explicitly mentioned in claim 1 as granted.

Consequently, the subject-matter of claim 1 of the main request which concerns the use of creatine and cyclocreatine and their pharmaceutically acceptable salts in the manufacture of a medicament for the treatment of, or preventing the occurrence of Huntington's disease or Parkinson's disease" is encompassed by claim 2 as granted. Additionally, the

scope of claim 1 of the main request is more restricted than that of claim 2 as granted, since the treatment of amyotrophic lateral sclerosis is no longer mentioned in the claim. Therefore, the requirements of Article 123(3) EPC are met.

3.1.3 Moreover, the first paragraph on page 41 of the application as filed provides a basis under Article 123(2) EPC for the subject-matter claimed in claim 1 of the main request, since it explicitly links the choice of creatine and cyclocreatine with the treatment of Huntington's disease and Parkinson's disease (this specific choice is further disclosed and illustrated in the examples of the application as filed). Moreover, the specific mention of creatine and cyclocreatine on page 41 of the application as filed can only be understood as reflecting the preferred choice for the active agent, which necessarily and generically includes the pharmaceutically acceptable salts mentioned on page 9 of the application as filed.

Therefore, claim 1 of the main request meets the requirements of Article 123(2) EPC.

3.2 Sufficiency of disclosure

The invention in claim 1 of the main request is disclosed in the patent in suit in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art.

Creatine and cyclocreatine, and their pharmaceutically acceptable salts, are known to the skilled person, and their specific uses, which are claimed in a second medical use claim in Swiss-type form (claim 1 of the main request), are specifically illustrated in the

examples by means of generally acknowledged models for Huntington's disease and Parkinson's disease (the malonate model and the MPTP model, respectively).

The appellant-opponent has not contested the sufficiency of disclosure of the invention according to the main request.

Therefore the main request meets the requirements of Article 83 EPC.

3.3 Novelty

3.3.1 Document D2 generically discloses compositions comprising creatine, and their use in the manufacture of a medicament (claims 1 and 11, pages 2 and 3 of D2). The fact that the compositions disclosed in document D2 comprise creatine and "a sugar", such as dextrose, fructose, glucose or maltose, does not change the fact that creatine is the active agent for which the medical uses are disclosed. The "sugar" and creatine (which are obtained separately from different providers as shown by the examples) are simply mixed when preparing the compositions (see the examples 1 to 3), and thus they are not present in the composition as inseparable intimate mixtures such as eutectic or molecular mixtures, nor are they in the form of a chemical entity such as a chemical complex. Therefore, the opposition division's analysis of document D2 is not correct in this respect.

The subject-matter of claim 1 of the main request is novel vis-à-vis document D2 since said document does not specifically disclose the use of creatine and its pharmaceutically acceptable salts for the treatment or

prevention of Huntington's disease and Parkinson's disease.

3.3.2 The subject-matter of claim 1 of the main request is novel vis-à-vis document D6 since the substituted guanidines and guanidine derivatives disclosed therein do not encompass creatine or cyclocreatine (see, in particular, the formula depicted on page 22 and the definitions for the rests and residues on pages 22 and 23 of document D6). The treatment of Huntington's disease is mentioned among other treatments in the last paragraph on page 16 of document D6, but this treatment is not disclosed together with creatine or cyclocreatine.

3.3.3 Claims 2 to 4 of the main request are dependent on claim 1, and their subject-matter is therefore also novel over the contents of documents D2 and D6.

3.3.4 The appellant-opponent has not objected to the novelty of the subject-matter claimed in the main request.

3.3.5 Consequently, the subject-matter claimed in the main request meets the requirements of novelty (Articles 52(1) and 54(2) EPC).

4. Request for overturning the opposition division's decision on apportionment of costs

The opposition division's decision to refuse the opponent's request for apportionment of costs under Article 104 EPC is correct. Under paragraph (1) of that article, each party to the opposition proceedings must bear the costs it has incurred, unless the opposition division, for reasons of equity, orders a different apportionment of costs. The opposition division

correctly found that the patentees' announcement made shortly before the date of oral proceedings that they withdrew their request for oral proceedings and would not be attending the oral proceedings did not amount to culpable conduct and could not be a factor in assessing whether reasons of equity for a different apportionment of costs under Article 104(1) EPC existed. In this way the patentees relied on the arguments they had presented in writing during the opposition proceedings and did not prevent the possibility of a decision being taken against their own interests at the end of the oral proceedings before the opposition division.

Moreover, the opposition division also correctly considered that the opponent had requested oral proceedings on an auxiliary basis for the eventuality that the patent was not revoked on the basis of its written submissions.

Additionally, the appellant-opponent, in the oral proceedings before the board, confirmed that the oral proceedings before the opposition division had served to defend its interests. Moreover, it did not dispute that essential arguments against the patentees' higher-ranking requests before the opposition division were presented and discussed for the first time at the oral proceedings before the opposition division.

Consequently, the request for overturning the opposition division's decision on apportionment of costs under Article 104 EPC is to be refused.

5. *Remittal (Article 111(1) EPC)*

The present decision is based on a new set of claims which was filed for the first time on appeal, on

28 October 2010, as auxiliary request 8. Claim 1 of the main request addresses the treatment and prevention of only two specific diseases: Huntington's disease and Parkinson's disease.

In this respect the board of appeal notes that the purpose of the appeal procedure is mainly to review the first-instance decision underlying the appeal.

Claim 1 of the main request does not relate to a composition, but to a second or further medical use for creatine and cyclocreatine (and their pharmaceutically acceptable salts). Therefore, the opposition division's approach to establishing the relevance of the prior art is flawed since the question to be asked is not whether the compositions of document D2 contained a sugar in addition to creatine. Inventive step has to be evaluated using a correct problem-solution approach and for this to become true the technical teaching disclosed in the prior-art documents on file has to be assessed in depth.

The appellant-opponent's arguments against remittal to the department of first instance have to be rejected since that department may be convinced that the appellant-opponent's arguments against inventive step are of a simple nature, but this does not mean that the assessment of inventive step is a simple question.

Therefore, after due consideration of all the circumstances underlying the present case, the board remits the case to the department of first instance for further prosecution on the basis of the main request, which is the set of claims filed as auxiliary request 8 on 28 October 2010.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution on the basis of the main request.

3. The request for overturning the opposition division's decision on apportionment of costs is refused.

The Registrar: The Chairman:

N. Maslin U. Oswald

Decision electronically authenticated