**Internal distribution code:**

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

# Datasheet for the decision of 17 December 2019

**Case Number:** T 1047/17 - 3.3.07

**Application Number:** 04711966.4

**Publication Number:** 1603578

**IPC:** A61K9/08, A61K31/737, A61P13/10, A61K33/14, A61K9/00

**Language of the proceedings:** EN

**Title of invention:**
TREATMENT OF INTERSTITIAL CYSTITIS WITH HIGH DOSE CHONDROITIN SULFATE

**Patent Proprietor:**
Aralez Pharmaceuticals Canada Inc.

**Opponents:**
Farco-Pharma GmbH
IBSA Institut Biochimique SA

**Headword:**
TREATMENT OF INTERSTITIAL CYSTITIS WITH HIGH DOSE CHONDROITIN SULFATE/Aralez Pharmaceuticals Canada Inc.

**Relevant legal provisions:**
RPBA Art. 12, 13
EPC Art. 54, 56

**Keyword:**
Admission of documents (yes)
Admission of requests (yes)
Main request - Novelty (Yes)
All requests - Inventive step (No)

**Decisions cited:**

**Catchword:**

Europäisches Patentamt
European Patent Office
Office européen des brevets

**Beschwerdekammern**

**Boards of Appeal**

**Chambres de recours**

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

**Case Number: T 1047/17 - 3.3.07**

# D E C I S I O N
# of Technical Board of Appeal 3.3.07
# of 17 December 2019

| | |
|---|---|
| **Appellant:** (Patent Proprietor) | Aralez Pharmaceuticals Canada Inc.<br>544 Egerton Street<br>County of Middlesex ON N5W 3Z8 (CA) |
| **Representative:** | Appleyard Lees IP LLP<br>15 Clare Road<br>Halifax HX1 2HY (GB) |
| **Respondent:** (Opponent 1) | Farco-Pharma GmbH<br>Gereonsmühlengasse 1-11<br>50670 Köln (DE) |
| **Representative:** | Von Rohr Patentanwälte Partnerschaft mbB<br>Rüttenscheider Straße 62<br>45130 Essen (DE) |
| **Respondent:** (Opponent 2) | IBSA Institut Biochimique SA<br>Pambio-Noranco (CH) |
| **Representative:** | Gerli, Paolo<br>Botti & Ferrari S.r.l.<br>Via Cappellini, 11<br>20124 Milano (IT) |
| **Decision under appeal:** | **Decision of the Opposition Division of the European Patent Office posted on 29 March 2017 revoking European patent No. 1603578 pursuant to Article 101(3)(b) EPC.** |

**Composition of the Board:**

| | |
|---|---|
| **Chairman** | A. Usuelli |
| **Members:** | D. Boulois |
| | Y. Podbielski |

## Summary of Facts and Submissions

I. European patent No. 1 603 578 was granted on the basis of a set of 10 claims.

II. The patent was opposed under Article 100 (a), (b), (c) EPC on the grounds that its subject-matter lacked novelty and inventive step, was not sufficiently disclosed, and extended beyond the content of the application as filed.

III. The appeal lies from the decision of the opposition division to revoke the patent. The decision was based on the claims as granted as main request, on auxiliary requests 1-3 filed with letter of 16 December 2016 and on auxiliary requests 4 and 5 filed during the oral proceedings before the opposition division on 17 February 2017.

Independent claim 1 of auxiliary request 4 read as follows:

"1. A pharmaceutical composition for use in the treatment of a human patient afflicted with interstitial cystitis or related conditions of the bladder and/or urinary tract by administration by instillation into the bladder of the patient wherein the related condition is a GAG-deficient form of cystitis, the composition comprising a unit dose of chondroitin sulfate in an amount of from 400mgs to 1200mgs, and an aqueous vehicle."

IV. The documents cited during the opposition proceedings included the following:

A1: US 6083933 A (D1 in the appeal proceedings)

A4: JP 2001 213784 A (English translation)
A10: Steinhoff et al.: "The efficacy of chondroitin sulphate in the treatment of interstitial cystitis and chronic inflammatory disease of the urinary bladder", The Canadian Journal of Urology, 9(1), Feb. 2002, pages 1454-1458
A13: CA 2 269 260 A1
A48: Dr Sorensen Declaration
A49: Dr Hurst Declaration
A56: Declaration of Professor J. Curtis Nickel
A79: Thakkinstian & Nickel, "Efficacy of intravesical chondroitin sulfate in treatment of interstitial cystitis/bladder pain syndrome (IC/BPS): Individual patient data (IPD) meta-analytical approach"; CUAJ, 7(5-6): 195-200.

V. According to the decision under appeal, documents A55 to A83 were admitted into the proceedings.

The main request and auxiliary requests 1-3 did not meet the requirements of Article 123(2) EPC.

Auxiliary request 4 met the requirements of Article 123(2) EPC, was sufficiently disclosed, and was novel over D1 and A4.

As regards inventive step of auxiliary request 4, D1 was seen as the closest prior art and disclosed the treatment of interstitial cystitis via instillation of chondroitin sulfate (CS) at doses of 200 mg or higher. Claim 1 of auxiliary request differed in the amount of administered CS, which was in the range of 400-1200 mg. The opposition division took the position that the experimental data provided in the contested patent did not allow for a comparison between the claimed dosage of 400-1200 mg and the 80 mg standard dosage used in

the prior art. The problem was reformulated as the provision of an alternative composition useful for treating interstitial cystitis. Since A1 envisaged dosages of 200 mg and higher, an inventive step could not be acknowledged. Moreover, as evidenced by A10, CS was known to be non-toxic even when administered in high amounts and A10 further clearly pointed to the fact that at least some patients could benefit if the dosage of CS and/or the frequency of treatments was increased.

Auxiliary request 5 was not inventive for the same reasons.

VI. The patent proprietor (hereinafter the appellant) filed an appeal against said decision. With the statement of grounds of appeal dated 8 August 2017, the appellant filed auxiliary requests 6 and 7 and submitted a new document:
A84: AM J. Clin. Exp. Urol., 2014, 2(3): 199-208.

VII. With letter dated 22 December 2017, opponent 01 (hereinafter respondent 01) requested that documents A55, A56, A58-A80, A81-A83 and A84 not be admitted into the proceedings.

VIII. With letter dated 28 June 2019, the appellant submitted a main request and auxiliary requests 1-2, and withdrew all previous requests on file.

Independent claim 1 of the main request was similar to claim 1 of auxiliary request 4, forming part of the appealed decision, except for the deletion of the term "of" before "from 400mgs".

Independent claim 1 of auxiliary requests 1 and 2 read as follows, difference(s) compared with claim 1 of the main request shown in bold:

Auxiliary request 1

"1. A pharmaceutical composition for use in the treatment of a human patient afflicted with interstitial cystitis or related conditions of the bladder and/or urinary tract by administration by instillation into the bladder of the patient wherein the related condition is a GAG-deficient form of cystitis, the composition comprising a unit dose of chondroitin sulfate in an amount from 400mgs to 1200mgs, and an aqueous vehicle, **wherein the chondroitin sulfate has a concentration of 20 mg/mL.**"

Auxiliary request 2

"1. A pharmaceutical composition for use in the treatment of a human patient afflicted with interstitial cystitis ~~**or related conditions of the bladder and/or urinary tract**~~ by administration by instillation into the bladder of the patient ~~**wherein the related condition is a GAG-deficient form of cystitis**~~, the composition comprising a unit dose of chondroitin sulfate in an amount from 400mgs to 1200mgs, and an aqueous vehicle, **wherein the chondroitin sulfate has a concentration of 20 mg/mL.**"

IX. In a communication pursuant to Article 15(1) RPBA, the Board stated in particular as regards inventive step that it was questionable whether an effect had been demonstrated over the closest prior art D1, and whether the claimed subject-matter was inventive over D1.

X. With a letter dated 1 October 2019, respondent 01 requested that the main request and auxiliary requests 1 and 2 not be admitted into the proceedings.

XI. Oral proceedings took pace on 17 December 2019.

XII. The arguments of the appellant may be summarised as follows:

Main request - Novelty

D1 was not novelty destroying, since it was not possible to combine the disclosed features of concentration and volume. Moreover, there was no example in D1 of a dose unit higher than 200mgs.

Main request - Inventive step

D1 was the closest prior art. There was no teaching in D1 of any improvement or expected benefit as regards the treatment of cystitis linked with a high dose unit of chondroitin sulfate. The skilled person had therefore no expectation of success when reading D1. It was therefore not obvious to higher the dose unit.

Figure 1 of the contested patent showed explicitly an improved effect, in particular when refractory patients were treated. No evidence had been provided that the positive results exhibited were invalid due to sample size. A noticeable improvement in symptomatology was exhibited in 5 of the 6 patients in the example of the application, and this showed that a clinically significant effect for a 400 mg dose of CS was superior to a 80 mg dose of CS.

Hence, the technical problem of providing an improved treatment was credibly solved.

This technical effect was confirmed by several practitioners in the following cited documents.

A49 showed that it was not expected that the saturation concentration of chondroitin sulfate in the bladder corresponded to a dose unit of about 400mg (see page 4).

A56 mentioned that the claimed dose units would work best in patients with a "bladder specific" clinical phenotype, confirming the efficacy of high doses (see page 2).

A79 mentioned also that the selection of appropriate patients for the chondroitin sulfate therapy would see an increased chance of the patient being classified as a chondroitin sulfate responder and also a better overall disease response in terms of decreased interstitial cystitis (see pages 199-200).

Declaration A48 also highlighted that a dose of 400 mg of chondroitin sulfate provided a more rapid and more significant improvement in treatment of symptoms of interstitial cystitis as shown by the contested patent.

The use of a higher dose unit of chondroitin sulfate would have led to a possible bladder irritation, and the physician would not have used such high doses.

The teaching of D1 could also not be combined with the teaching of A10, which mentioned that the dose could be increased up to 4 times, which was still less than 400 mg. There was no disclosure in A10 of a dose unit of

400 mg or more, and it was not clear from this document whether the physician could increase the dose unit or the frequency of administration.

Neither D1, nor A10 would have incited the skilled person to use a dose of 400 mg or higher, this indication could not be found in any of these documents. A10 did in particular not show any improvement linked to the use of a higher dose.

Auxiliary request 1 - Inventive step

Claim 1 had been restricted by a concentration value, which was 10 times higher than in the prior art. This constituted a further difference and was not obvious.

Auxiliary request 2 - Inventive step

Claim 1 was restricted to a specific disease, which was not disclosed in D10.

XIII. The arguments of the respondents may be summarised as follows:

Admission of the main requests and auxiliary requests 1-2 into the appeal proceedings

Respondent 01 objected to the admission of the requests since they had been late filed and were prima facie not allowable.

Admission of documents A55, A56, A58-A84 into the proceedings

Respondent 01 objected the admission of these documents into the proceedings. Documents A55, A56 and A58 to A83

should not have been admitted into the proceedings by the opposition division. Document A84 was late filed and not prima facie highly relevant.

Main request - Novelty

According to respondent 01, the "whole content approach" had to be applied to the disclosure of D1, which disclosed the treatment of cystitis by chondroitin sulfate. Column 3 of D1 mentioned that a useful dose of chondroitin sulfate was 200 mg or higher. Moreover the combination of the disclosed concentrations and volumes of the dose units on columns 3 and 4 led to a disclosure of a dose unit over 400 mg. The same disclosure could be found in claim 1 of D1 combined with claims 17-20. A dose unit of 400 mg to 1200 mg was therefore disclosed directly and unambiguously in D1.

According to respondent 02, D1 disclosed an overlapping teaching, with a dose unit of more than 200 mg, which was an interval with an open range. The selection of a range of 400 mg to 1200 mg could not be novel in view of the novelty requirements, applying to a selection from a range.

Main request - Inventive step

According to respondent 01, D1 was the closest prior art, and said document suggested to use high doses of chondroitin sulfate. The unique difference between the claimed subject-matter and the disclosure of D1 was the dose unit.

There was no evidence of any effect linked with the claimed dose unit. Moreover all sources cited by the

appellant were personal opinions or isolated observations. There was also no definition of what could be a refractory patient in the contested patent or in any cited document, and the definition of this term was only speculative.

There was no comparison made with the prior art, in particular with a dose of 200 mg as disclosed in D1.

As regards the tests presented in the contested patent and reflected in Figure 1, the sample used was not homogenous and too small, hence not representative. The comparison with a treatment at 80 mg per dose unit was also not valid, since the patient sample was not the same, and the severity of the symptoms was higher in the sample tested with the higher dose unit, which showed that the group of patients was different. The protocol of testing was also not given in the 80 mg dose unit group.

The example of the contested patent could not provide a valid comparison, since it did not focus on the distinguishing features, namely the dose unit, but also the volume of the dosage form and the concentration of CS.

The claimed solution of a dose unit of 400 to 1200 mg was obvious in view of D1 alone, and even more obvious in view of A10, which suggested to increase the dose units when the patient does not respond to the initial dose.

According to respondent 02, if a disease was complicated to treat, any improvement had to be shown rigorously, which was not the case here. Moreover, the dose of 80 mg was not presented in the prior art as a

maximum dose, but as a usual standard dose, and D1 suggested to increase said dose. Said dose of 80 mg provided the same effect than a dose of 400 mg, since the contrary had not been shown.

As regards the type of patients, there was no indication in the claims or the description of the contested patent which patients had responded to the high claimed doses. Moreover, the term "refractory patients" used in the test of the patent did not mean refractory to a dose of 80 mg, but refractory to other alternative treatments, and in the test disclosed in the patent this term related only to 2/3 of the patients.

Moreover, the clinical data provided in the patent could not demonstrate any improvement, and the curves in Figure 1 relative to the different dose groups were not comparable, since the patient group was small, different from the comparative group treated with 80 mg of CS, and the patent did not give any details on the treatment regimen followed by the reference 80 mg group.

Chondroitin sulfate was not a toxic product, since it did not pass to the blood circulation, and this was another element that would have incited the skilled person to increase the dose when necessary.

Auxiliary request 1 - Inventive step

According to respondent 01, the concentration was disclosed in D1 in column 3, and was an obvious feature.

Auxiliary request 2 - Inventive step

The arguments remained the same.

XIV. Requests

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 auxiliary requests 1 and 2, all filed with letter dated 28 June 2019.

Respondents 1 and 2 requested that the appeal be dismissed.

Respondent 1 also requested that neither the main nor the auxiliary requests nor documents A55, A56, A58-A84 be admitted into the proceedings.

## Reasons for the Decision

1. Admission of documents A55, A56, A58-A84 into the proceedings

1.1 Documents A55-A83 have already been admitted into the proceedings by the opposition division, since they were filed by the patent proprietor in reply to the notices of opposition (A55- A80) or in reply to the opponent's line of argument and before the deadline for submissions before the oral proceedings (A81-A83). Several of these documents are also mentioned in the decision of the opposition division (A59, A56, A79, A67, A72, A57).

Documents A55-A83 therefore form part of the proceedings.

1.2 A84 has been filed by the appellant with the statement of grounds of appeal, in response to the decision of the opposition division as regards inventive step. This document is cited to give technical information on the different types of cystitis in view of the disclosure of A10 which was mentioned by the opposition division in its decision as regards inventive step.

Consequently, the Board admits the document into the proceedings (Article 12 RPBA 2007).

2. Admission of the main request and auxiliary requests 1 and 2 into the appeal proceedings

2.1 The main request corresponds to auxiliary request 4 filed at the oral proceedings before the opposition division and maintained with the statement of grounds of appeal, but with independent claim 7 of that request deleted. Given that the subject-matter of claim 1 of this request is in substance identical to claim 1 of auxiliary request 4 filed in the opposition proceedings, on which the decision of the opposition division was based, the Board decides to admit it into the proceedings (Article 13 RPBA 2007).

2.2 Auxiliary request 1 corresponds to auxiliary request 6 filed with the grounds of appeal, with claims 2 and 7 of that request cancelled and with the following modification in claim 1: "wherein the chondroitin sulfate has a concentration of 20mg/mL" instead of "2.0% weight/ volume", which has an identical technical meaning, and therefore does not present any new issue or complexity. Since the request had, in essence, been filed at the earliest stage of the appeal proceedings, and in response to the decision of the opposition

division, the Board admits it into the appeal proceedings (Article 13 RPBA 2007).

3. Auxiliary request 2 corresponds to auxiliary request 6 filed with the statement of grounds of appeal, with a rewording for clarity and independent claim 7 deleted. Claim 1 of auxiliary request 2 corresponds also to claim 1 of auxiliary request 1 with the deletion of the feature "or related conditions of the bladder and/or urinary tract by administration into the bladder wherein the related condition is a GAC-deficient form of cystitis". In view of the limiting and uncomplex nature of this amendment, the Board decides to admit the request into the appeal proceedings (Article 13 RPBA 2007).

4. Main request - Novelty

4.1 Respondent 01 objected a lack of novelty over D1, A4 and A13.

D1 discloses the treatment of cystitis by a unit dose of chondroitin sulfate (CS) of up to about 200 mg, especially as a 2 mg/mL dose in a buffer volume of 40 mL (see the example); D1 mentions in col. 3, lines 40-42, that a useful dose can be 200 mg and higher, without further specification.

The document discloses in a further passage that the volume of the formulation may be up to 100 mL (see col. 3, lines 47-55). Said passage does however not link this volume amount to any weight amount or concentration of CS.

In another distinct passage, the document discloses also that the concentration of CS in the solution lies

within the range from 0.1 mg/mL to 100mg/mL, preferably 1.0 mg/mL to 20 mg/mL (see col. 3, l. 63 - col. 4, l. 1); said passage does however not link this disclosure to any volume amounts of the solution, except the final part of the passage stating that the preferred embodiment is a formulation with 80 mg of CS in a 40 mL volume, i.e having a concentration of 0.2 mg/ml (0.2%).

Finally, the disclosure of a solution comprising CS in a concentration of 2 mg/mL, is also not linked with a disclosure of volume amount, except with the specific volume amount of 40 mL (see col. 4, lines 9-12 and lines 29-31.

Consequently, this document does not disclose explicitly or implicitly a unit dose of 400 mg or higher and therefore cannot be relevant for novelty.

The content of a prior art document can indeed not be assimilated to a reservoir from which it would be permitted to draw characteristics presented independently together and create thereby a particular artificial embodiment which would destroy the novelty, unless the document itself suggests a such combination. This is not the case here. The passages dealing with the concentration of CS are presented independently from the passages dealing with volume amounts of the solution, and cannot be combined to create an artificial embodiment.

4.2 A13 has the same disclosure as D1, and it is thus also not relevant for novelty.

4.3 A4 concerns the treatment of cow's mastitis and cannot be relevant for novelty for this reason.

4.4 Consequently, the main request meets the requirements of Article 54 EPC.

5. Main request - Inventive step

5.1 The invention relates to a composition for use in the treatment of interstitial cystitis or related conditions of the bladder and/or urinary tract by instillation of chondroitin sulfate (CS) into the bladder of the patient in an amount of 400 to 1200 mg.

5.2 The closest prior art is D1, which relates to the same use. The dose of CS used is up to 200 mg, in particular comprised between 40 to 120 mg, and in a specific embodiment of the invention, it is 80 mg (col. 3, l. 37-47). Said document mentions also that a useful dose can be 200 mg or higher (see col. 3). This document does therefore not disclose a unit dose of 400 to 1200 mg.

5.3 According to the appellant, the problem is the provision of an improved treatment for interstitial cystitis.

According to the respondents, the problem is the provision of an alternative treatment of interstitial cystitis.

5.4 As a solution to either problem, claim 1 of the main request proposes a unit dose of chondroitin sulfate in the particular amount of 400 to 1200 mg.

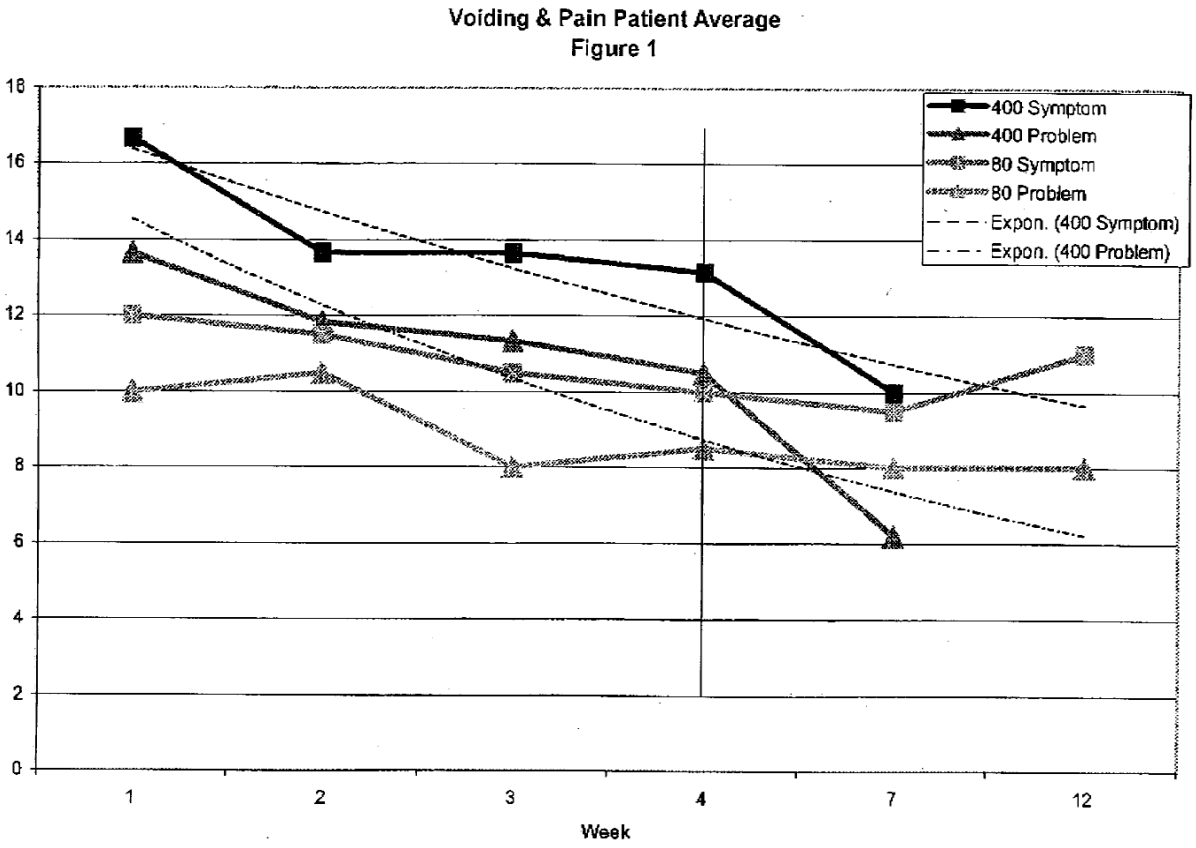
5.5 It has to be investigated whether there is sufficient evidence supporting the alleged effect of an improved treatment.

5.5.1 The appellant relies on experiments disclosed in the contested patent and in the disclosure of several documents, namely A49, A56, A48, A79 to show that the claimed dose unit involves an improved treatment of interstitial cystitis by CS. A10 is also mentioned by the appellant to highlight what was the standard dose unit before the filing date of the contested patent.

5.5.2 Experiments of the contested patent

The description of the contested patent discloses the treatment of 6 patients with either weekly or twice weekly administration of 400 mg of CS (see par. [0037]-[0044] of the patent specification). Four of the chosen patients were refractory to other forms of treatment, one patient was said to be in a flare-up while on taking pentosan polysulfate sodium (Elmiron®) and one was new to treatment (see par. [0043]). The description discloses further in paragraph [0045] and Figure 1 a comparison as regards the improvement in voiding and pain seen, between the population of patients treated with 400 mg of CS, vs a population treated with 80 mg/ 40 mL of CS. The assessment is made using the Oleary scoring system, and paragraph [0045] mentions that the population treated with 80 mg of CS was "a different interstitial cystitis patient population".

Figure 1 shows the following:




In the Board's view, these experiments do not demonstrate an improved treatment linked with a dose unit of 400mgs or more. The main reason is that the patient groups treated with 400 or 80 mg were not equivalent, and constitute indeed "different interstitial cystitis patient populations" as mentioned in the contested patent. As it can be observed in Figure 1, the starting level of symptomatology, expressed as voiding and pain, is higher in the 400 mg group (a level of about 14 and 16) than in the 80 mg group (a level of about 10 and 12). A comparison as to the effect of the two treatments is therefore not possible, since the tested populations are different, i.e. the population treated with 400 mg had a more severe interstitial cystitis than the population treated with 80 mg. Moreover, this study does not show any comparison with a dose higher than 80 mg, such as 200 mg as suggested in D1.

In addition, there is no indication of how the data of Figure 1 were obtained concerning the improvement made by the group of 6 patients treated with 400 mg, in particular whether the results expressed in Figure 1 relate to the 6 patients or only some of them, especially in view of the absence of reaction to the treatment of the patient number 1. An improvement was indeed noticed for patients 2, 3 and 4 of the study while a moderate improvement was noticed for patients 5 and 6, and no improvement was noticed for patient 1.

The same considerations apply to the comparative 80 mg group, since there is no information and data as to how the results for this patient group has been obtained. In particular, no information is given as to the protocol of administration and the dosage.

Consequently, the experiments and clinical data of the contested patent cannot provide a valid comparison, and accordingly cannot demonstrate that a dose amount of 400 mg or more of CS provides an improved treatment or any other effect over a dose unit as disclosed in D1.

5.5.3 Other documents

Other documents were cited by the appellant to corroborate the experiments of the contested patent:

- A49 is a physician's declaration which mentions that the usual dose of 80 mg of CS was initially considered to be more than sufficient to treat cystitis by replacing the normal GAG layer on the surface of the bladder. A further study revealed however that a damaged bladder results in a exposure of a larger volume of tissue, thus requiring much more CS than was

previously expected (see par. 7, and Exhibit A). The doses of 80 and 200 mg of CS were below the saturation level of the damaged bladder, which was reached only with a dose of at least 375 mg (see par. 8 and Exhibit B).

- A56 is also a physician's declaration, which relates to the use of instilled doses of 2% CS in 20 mL, hence a dose unit of 400 mg. Without providing experimental data, the physician indicates that, in his opinion, this dose was more effective than the standard 80 mg dose (see par. 5 ). Said declaration suggests also that said dose works best in patients with a "bladder specific" clinical phenotype, that is patients with urgency and frequency whose major symptom is related to pain perceived to be in the bladder (cf. par. 4).

- A48 is also a physician's declaration, which highlights that a dose of 400 mg of chondroitin sulfate provided a more rapid and more significant improvement in treatment of symptoms of interstitial cystitis (see par. 5). It also states that a increase of the dose unit to 800 mg of CS does not appear to provide further improvement (see par. 8).

- A79 is a meta-analysis which confirms that the intravesical administration 2% of CS (400 mg) is an effective therapy for some patients with interstitial cystitis, with significant more benefit than a placebo.

- A10 is a study analyzing the efficacy of a standard 0.2% CS solution of 40 mL, containing therefore 80 mg of CS, in the treatment of interstitial cystitis.

The Board finds that none of these documents provides a comparison between different unit doses of CS in the

treatment of interstitial cystitis so that an effect of improved treatment for interstitial cystitis linked with a dose of 400 mg or higher is not proven. In view of the physician's opinions A48, A49 and A56, it might be possible that a unit dose of 400 mg has a beneficial effect over lower doses of CS on selected specific patients with particular severe symptoms, but this remains unproven and said possible responsive patients are neither defined in any cited document or in the contested patent, nor are they claimed.

5.5.4 In the absence of any proof of improved treatment of interstitial cystitis, the problem has to be formulated as it was defined by the respondents, namely the provision of an alternative treatment of interstitial cystitis. In view of the experiments shown in the contested patent, the problem is convincingly solved.

5.6 The claimed solution, i.e. a unit dose of 400 mg to 1200 mg, appears obvious for the reasons given below.

In the Board's view, in the present specific case, if the skilled person is confronted with an unsatisfactory therapy result of the treatment of interstitial cystitis as disclosed in D1, he would increase the CS doses and would administer it over a longer period of time. The use of increased doses of a medicament to improve its efficacy is indeed an immediately evident measure a skilled person would take and the relief of patients with more severe symptoms by a higher dose of a medicinal agent cannot constitute an unexpected or surprising effect.

This is expressed in D1 which discloses explicitly that "the unit dose of CS suitable for administration to the patient may vary depending on the severity of the

condition...a useful dose for an adult afflicted with interstitial cystitis can be 200 mg or higher" (see D1, col. 3, lines 37-43).

It is also emphasized in A10, which suggests in specific unresponding patients "an increased dosage of chondroitin and/or an increase in the frequency of treatments. Starting more than two years ago, we began treating IC patients by instilling chondroitin sulfate and have also used dosages of 4 times the normal dose to treat chemical and radiation induced cystitis"; A10 adds that "modifying a patient's treatment regime and dosing regimen according to individual symptoms may prove to be even more effective" (see A10, page 1457).

A skilled person would all the more increase the dose unit of CS in the treatment of interstitial cystitis, since it is known that CS does not present any particular toxicity, as known for instance from A10 (see page 1457).

5.7 Consequently, in the present case, the adaptation of the dose unit to the patient or to the severity of the disease is considered to be a matter of routine experimentation and cannot be seen as involving an inventive step. The main request does not meet the requirements of Article 56 EPC.

6. Auxiliary request 1 - Inventive step

Claim 1 of auxiliary request 1 has been restricted by the feature "wherein the chondroitin sulfate has a concentration of 20 mg/mL".

There is no particular effect linked with this feature, and D1 suggests such a concentration , namely a

concentration of CS comprised between 0.1 and 100 mg/mL, preferably 1.0 mg/mL to 20 mg/mL (see col. 3 last par. - col 4, first par.).

The amendment introduced in claim 1 has therefore no impact on the assessment of inventive step, and auxiliary request 1 does not meet the requirements of Article 56 EPC for the same reasons as the main request.

7. Auxiliary request 2 - Inventive step

In comparison to claim 1 of auxiliary request 1, claim 1 of auxiliary request 2 has been further restricted to an unique medical indication, namely "a pharmaceutical composition for use in the treatment of a human patient afflicted with interstitial cystitis".

Since D1 also relates to the treatment of interstitial cystitis, this restriction has no bearing on the assessment of inventive step. The conclusions reached for the main request and auxiliary request 1 apply mutatis mutandis also for this request.

Auxiliary request 2 does not meet the requirements of Article 56 EPC for the same reasons as the main request.

## Order

## For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

B. Atienza Vivancos A. Usuelli

Decision electronically authenticated