England and Wales High Court (Patents Court) Decisions

Neutral Citation Number: [2016] EWHC 24 (Pat)
Case No: HP-2014-000011

IN THE HIGH COURT OF JUSTICE
CHANCERY DIVISION
PATENTS COURT

Royal Courts of Justice
Strand, London, WC2A 2LL
13/01/2016

B e f o r e :

THE HON. MR JUSTICE BIRSS

Between:

ACCORD HEALTHCARE LIMITED	**Claimant**
- and -	
MEDAC GESELLSCHAFT FÜR KLINISCHE SPEZIALPRÄPARATE MBH	**Defendant**

Adrian Speck QC and Lindsay Lane (instructed by Taylor Wessing) for the Claimant
Charlotte May QC and Mark Chacksfield (instructed by Bristows) for the Defendant
Hearing dates: 23rd, 24th, 26th November 2015

HTML VERSION OF JUDGMENT

Mr Justice Birss:

Introduction

1. This is a case concerning patent EP (UK) 2 046 332, entitled "Concentrated Methotrexate Solutions". The patent claims the use of a formulation of methotrexate with a concentration of about 50 mg/ml for the treatment of individuals with inflammatory autoimmune diseases by subcutaneous injection. The point of the invention is that known concentrations of methotrexate used for this indication were at a lower level (no more than 25 mg/ml) and so by using a higher concentration of the drug, the injection volume can be reduced and so the injection will be less painful.

2. The patent has a priority date of 21st July 2006. The patent was originally filed and granted in the German language. The English translation is agreed.

3. The proprietor of the patent is the defendant, medac. The company writes its name with a lower case "m". In this judgment I will use the lower case form of the name unless the word appears at the start of a sentence. Medac is a privately owned German company which promotes the development and marketing of therapeutics in malignant diseases, particularly therapeutics for use in treating cancer and autoimmune diseases. This patent protects medac's Metoject® syringe and pen products. These were launched in the UK in 2008 and are now widely used in the treatment of rheumatoid arthritis (RA) and related inflammatory conditions.

4. The claimant in this action is Accord, a generic company. It is seeking to clear the way in order to launch its own 50 mg/ml injectable product. Accord claims that the patent is invalid; medac contends that the patent is valid.

The issues

5. Claims 1, 13, 15 and 27 have been asserted as independently valid by medac. They are as follows:

> Claim 1: Use of methotrexate for the production of a medicament to be administered subcutaneously for the treatment of inflammatory autoimmune diseases, wherein the methotrexate is present in a pharmaceutically acceptable solvent at a concentration of about 50 mg/ml.
>
> Claim 13: Use according to claim 7, wherein the ready-made syringe contains a dosage of 5 to 40 mg, in particular 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, 20.0, 22.5, 25.0, 27.5, 30.0, 32.5, 35.0, 37.5 or 40.0 mg, of methotrexate.
>
> Claim 15: Methotrexate for use in the treatment of inflammatory autoimmune diseases, wherein the methotrexate is to be administered subcutaneously and the methotrexate is present in a pharmaceutically acceptable solvent at a concentration of about 50 mg/ml.
>
> Claim 27: Methotrexate for use according to claim 21, wherein the ready-made syringe

contains a dosage of 5 to 40 mg, in particular 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, 20.0, 22.5, 25.0, 27.5, 30.0, 32.5, 35.0, 37.5, or 40.0 mg, of methotrexate.

6. Claims 13 and 27 are dependent on intermediate claims (7 and 21) between claims 1 to 13 and 15 to 27 respectively. Those intermediate claims provide that the concentrated methotrexate solution is contained in a ready-made syringe.

7. Claims 1 and 13 are Swiss form claims, claims 15 and 27 are purpose limited product claims (EPC 2000). Nothing turns on this and no issues of claim construction arise in this case.

8. The issues are:

    i) *Obviousness* in the light of:

        a) The common general knowledge alone;

        b) A paper "*Methotrexaat buiten de kliniek*" by Jansen et al. (1999) Pharmaceutisch Weekblad, Volume 134, No 46, p1592 (Jansen). The original language of the paper is Dutch. There is an agreed translation;

        c) A letter "*Tolerance of parenteral, higher dose methotrexate in children with juvenile chronic arthritis*" by Russo and Katsicas (2000) Clinical and Experimental Rheumatology, Volume 18, No 3, p425, (Russo);

        d) The fact that the patent encompasses embodiments which make no technical contribution. This is directed to claims 1 and 15 which provide no limitation on volume. Accord argues that some of the products within the claim offer no pain reduction advantage over the prior art and therefore the claim encompasses embodiments which make no technical contribution.

    ii) *Insufficiency*. The argument is that the patent does not render it plausible that the claimed concentration could be safely administered to patients. This is a squeeze on inventive step.

The witnesses

9. Accord called two experts: a clinician and a formulator. Medac called an expert clinician only.

10. Accord called Dr Andrew Östör as its expert clinician. Dr Östör is a Consultant Rheumatologist and Director of the Clinical Research Unit at Addenbrooke's Hospital in Cambridge. He is an Associate Lecturer in the Faculty of Clinical Medicine at the University of Cambridge. He is also a Fellow of the Royal College of Physicians in London and Edinburgh respectively.

11. Accord called Dr Peter Rue as its expert formulator. Dr Rue is a Visiting Professorial Fellow to the Department of Pharmacy of the University of Aston in Birmingham. He also currently acts as a commercial pharmaceutical consultant. He has many years of experience working in formulation and development in industry. His experience includes having worked as Head of the Pharmaceutical Development Department at Glaxo Research and Development from 1990 to 1995.

12. Medac called Professor Ulf Müller-Ladner as its expert. Prof Müller-Ladner is currently Director of the Department of Rheumatology and Clinical Immunology at the Kerckhoff Clinic in Bad Nauheim. He is also Professor of Internal Medicine and Rheumatology at the Justus Liebig University Giessen and President of the German Society of Rheumatology for the year 2015-2016. Prof Müller-Ladner has previously worked with medac in a number of capacities, including as a consultant and as a member of its research advisory board. He has also acted as an expert witness for medac in a US action in respect of a related patent to EP 2 046 332 (US Patent No.8 664 231). Prof Müller-Ladner is a native German speaker but gave his evidence in English.

13. Each witness gave their oral evidence fairly, aiming to assist the court. The parties made detailed submissions about aspects of each witness's evidence but they are best dealt with in context.

The person skilled in the art

14. One of the important disputes in this case concerns the identity of the person skilled in the art. Accord submitted that the skilled person is a team consisting of a clinician, specialising in the field of inflammatory autoimmune diseases such as RA, and a formulator. The team may also include a nurse and a pharmacist although these latter two are not the focus of the controversy. Medac submitted that the skilled person is the clinician alone. The identity of the clinician following medac's approach is the same as Accord's. The major issue is about the position of the formulator. Accord submits it is plain from the patent itself that it is directed to a team consisting of a clinician and a formulator. So the skilled person is such a team.

15. Looking ahead to medac's case on obviousness, it makes the following submissions. Medac argues that the formulator would only be brought into a team at the instigation of the clinician, that it would not be obvious to the clinician to think there was any need to produce a new formulation of subcutaneous methotrexate and so the clinician would not approach a formulator at all. Therefore it is unfair to define the team as a team consisting of a clinician and a formulator from the outset. To do so is to fall into the trap identified by the Court of Appeal in ***Schlumberger v EMGS*** [2010] EWCA Civ 819 in that it may involve hindsight to postulate a team consisting of two distinct disciplines which had not been put together in reality before the priority date. The fact that, given the patent, one would put the two disciplines together into a team in order to implement the teaching does not mean that that team is the correct person skilled in the art for the purposes of obviousness. Medac also contends that the way in which Accord put its case in evidence was on the basis that impetus came from the clinician and so it is not legitimate to allow Accord to change its case in closing after the evidence had been heard.

16. Starting with the general law: a patent is directed to those persons likely to have a practical interest in the subject matter (see e.g. ***Medimmune v Novartis*** [2012] EWCA Civ 1234 at paragraphs 72 and 76). In appropriate cases the skilled person can be a team.

17. ***Schlumberger*** shows that the skilled person in the context of obviousness is not necessarily the same as the skilled person from the point of view of reading and implementing the patent. In paragraphs 55 and 63 of his judgment in ***Schlumberger*** Jacob LJ (with whom Sullivan and Waller LJ agreed) explained that while it was generally true that the same person/team would be considered for both purposes, it was not necessarily so as a matter of law.

18. What are the legal principles which govern the question ofwhether the skilled person or skilled team are the same for both purposes or not? The court in ***Schlumberger*** identified the following aspects as

relevant. First, if an invention brought together two disparate fields and was therefore "art changing", then the identities of the person/team from the two different perspectives may be different (Jacob LJ paragraphs 55 and 64). Second, (paragraph 65) the court explained that a key question is generally – what problem was the patentee trying to solve? That leads one to consider the art in which the problem lay. It is the notional team in that art which is relevant. Third, you cannot assume that a person in one field would know what was known by a person in another field, proof is required (paragraph 70). Fourth, and importantly in my judgment, the skills (and mind sets) of real persons or teams in the art are what matter when one is constructing the notional skilled person/team to whom the invention must be obvious if the patent is to be found invalid (paragraph 42).

19. The evidence of both Dr Östör and Dr Rue was that the skilled person was a team consisting of a clinician and a formulator. Prof Müller-Ladner's evidence was that the patent was addressed primarily to a clinician and that they would be able to call on the expertise of other people such as formulators and pharmacologists.

20. On the question of the person to whom the patent is addressed, in my judgment Accord is correct and I prefer the evidence of Dr Östör and Dr Rue on the issue. The document itself is not directed to a clinician alone who may or may not choose to involve a formulator. It is directed to a team in which the clinician and the formulator are working together. Formulation is at the heart of the matter. The invention is the use of a new dosage form of a known drug (methotrexate) to treat diseases it is already indicated for (RA and other diseases) using a known mode of administration (subcutaneous). The new dosage form is a formulation of the drug in a solvent at a particular concentration (about 50 mg/ml). The patent is plainly addressed to such a team in a pharmaceutical manufacturer. After all that is where formulators work and that is where these new dosage forms come from. Prof Müller-Ladner accepted in cross-examination that the patent is directed to industry. It is common ground that the clinician will be someone with experience of treating patients, but for the purposes of considering this patent, they will work with the formulator.

21. Turning to the question of the skilled person/team for the purposes of obviousness, I will address the factors mentioned in ***Schlumberger***. I am satisfied that such teams existed in reality irrespective of the patent. Prof Müller-Ladner accepted that there were companies which might wish to make methotrexate products to compete with those already on the market and accepted that a skilled team working in industry would typically include a formulator and a clinician. Therefore the existence of such a team is not an assumption, it is based on the evidence. Moreover this is not a case in which the invention is "art changing" or has brought together two disparate fields.

22. Consideration of the problem(s) which the invention aims to solve raises a number of issues. The patent is directed to the problem of pain. The problem to be solved described in the document is pain on subcutaneous injection caused by a relatively large volume of drug being injected. The solution is a higher concentration of methotrexate which therefore permits a lower volume to be used for a given dose. Another aspect of the problem advanced by the patentee at trial (albeit not mentioned in the patent) is a concern about possible side effects due to the higher concentration deterring the skilled person from going forwards or at least meaning that there was not a sufficient expectation of success in the testing which would be required to make the invention obvious. Finally another aspect of the patentee's case is that the skilled person would not think there was a problem to solve at all. Taking these issues into account does not mean that the skilled person/team should be considered as a clinician alone rather than a team.

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