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Actavis v. Merck: A Dosage Regime is not Patentable

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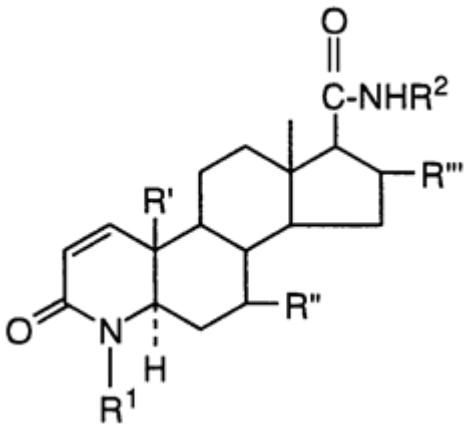

Merck & Co. is a company governed by the laws of the United States of America and the owner of European patent EP 0 724 444, filed on 11 October 1994, which relates to a “method of treating androgenic alopecia with 5? reductase inhibitors”.

Main claim 1 of the patent is worded as follows: “The use of 17ß-(N-tert-butylcarbamoyl)-4-aza-5-alpha-androst-1-ene-3-one for the preparation of a medicament for oral administration useful for the treatment of androgenic alopecia in a person and wherein the dosage amount is about 0.05 to 1.0 mg”.

This claim drafted in the Swiss-type format (which was under EPC 1973, the only possible way of protecting inventions relating to second medical uses, but which no longer exists under EPC 2000 since Article 54(5) EPC 2000 now expressly permits the patentability of further medical uses; see EPO, 19 February 2010, G2/08, *OJ EPO* 2010, p. 456) sets out three main characteristics: 1) use of finasteride for the preparation of a medicament for oral absorption, 2) useful for treating androgenic alopecia, 3) the (daily) dose of the active ingredient finasteride ranging from 0.05 to 1 mg.

Actavis, company governed by the laws of Iceland, specialised in the manufacture and distribution of pharmaceutical products brought proceedings against Merck & Co. requesting that the *Tribunal de Grande Instance* of Paris hold claims 1, 2 and 3 of the French designation of Patent EP 0 724 444 invalid for lack of industrial application, for lack of novelty and for lack of inventive step.

In a judgment dated 28 September 2010, the *Tribunal de Grande Instance* of Paris held that

claims 1, 2 and 3 of the French designation of Merck & Co. Ltd's Patent EP 0 724 444 were invalid for being excluded from the scope of patentability in accordance with the provisions of Article 53(c) EPC 2000 (former Article 52 (4) EPC 1973). The court held that the invention the subject-matter of the main claim 1 was only a new dosage regime ranging from 0.05 to 1 mg) of an already known compound (finasteride) in an already known therapeutic application (the treatment of hyperandrogenic conditions and especially the treatment of androgenic alopecia). A mere new dosage regime is not a second medical use but a therapeutic method excluded from patentability pursuant to Article 53 (c) EPC 2000.

Firstly, the court exposed the basic knowledge necessary to understand the claimed invention. Androgenic alopecia is the phenomenon which involves the lowering of hair density or complete loss of hair related to the excessive accumulation of androgen hormones and in particular of testosterone. The enzyme 5?-REDUCTASE is found upstream of this androgenic alopecia process since it has the effect of producing the hormone 5?-DIHYDROTESTOSTERONE–DHT- which is itself the principal mediator of androgenic activity. Then androgenic alopecia can be stopped or prevented through the use of an inhibitor of the 5?-REDUCTASE, such as the active ingredient known as finasteride (also named 17ß-(N-tert-butylcarbamoyl)-4-aza-5?-androst-1-ene-3-one).

Secondly, the court held that, in light of the prior art, the invention the subject-matter of claim 1 was new only owing to a specific dosage regime. In 1985, Merck & Co. itself had filed a patent disclosing the use of finasteride as a compound to treat hyperandrogenic conditions by oral or topical administration; and in 1988 it had filed another patent disclosing the use of finasteride by topical administration for treating androgenic alopecia which is also a hyperandrogenic condition. Consequently, the use of finasteride as a medicament to treat androgenic alopecia, with various possible methods of administration (topical or systemic), was already part of prior art before the filing of Patent EP 0 724 444. Both the active ingredient and its use for treating a specific illness (androgenic alopecia) were already well known. And finally only the dosage regime of this active ingredient, ranging from 0.05 to 1 mg whereas the earlier patents considered certain specific dosages ranging from 5 to 2,000 mg, was new and claimed as protectable by Patent EP 0 724 444.

The court then explained that a specific dosage regime is not a medical use but a therapeutic method excluded from patentability pursuant to Article 53 (c) EPC 2000.

A specific dosage regime is not a medical use because a medical use is the use of a substance in order to treat a specific illness whereas the dosage regime is nothing else but a choice, within the frame of one medical use (the use of one substance to treat one illness), of a precise dosage within a range of efficacious dosages. Consequently, "a specific dosage for the treatment of an illness constitutes neither a first nor a second therapeutic application but simply an indication of the range within which this substance is efficacious so as to treat such or such an illness in light of the tests and research completed and explained in the patent".

And a specific dosage regime is a therapeutic method, excluded from patentability by Article 53 (c) EPC 2000 because the dosage regime, *i.e.* the determination of the ideal amount of active ingredient used for treating one illness, is a factor that the practitioner has the task of determining in his therapeutic approach by confronting his theoretical knowledge in the field of illnesses and medicaments with many other factors (such as age, weight and gender of the patient, history and other illnesses, other treatments followed) which define the particular case of his patient. On this occasion, the court underlined that the dosages recommended in the leaflets of medicaments are merely indicative and only the doctor, in a therapeutic approach, has the right to prescribe the

dosage adapted to each patient.

“Consequently, it is possible to patent a medicament for the treatment of a first and then a second illness but not a dosage adapted to the treatment of those illnesses as by doing so, one attempts to patent a therapeutic method, which is excluded in order to belong to the field of care and to depend only on the concomitant freedom and responsibility of each doctor”.

The *Tribunal de Grande Instance* of Paris is thus inspired by a purposive interpretation of Article 53 (c) EPC 2000. The exclusion of the therapeutic methods from the scope of patentability is due to the will to preserve the practitioner’s freedom in the practice of the medical art. The legislator intended to make what is the core of the medical art unavailable for commercial purposes and wanted medical doctors to remain free in exercising their art. The way in which the practitioner performs his diagnosis and chooses the therapy which he prescribes is not patentable so as not to be hampered by the existence of patents. However, as noted by the court, the determination of a dosage is necessarily one of the steps that allow the practitioner to make a decision about the medical treatment to be given, and the dosage is one element of the therapeutic method implemented by the practitioner exercising the medical art. In this sense, the *Cour d’Appel* of Paris has already defined the method of therapeutic treatment as “a set of rational, consistent and connected procedures made by the skilled man and intended to discover means of preventing, treating, relieving, resolving or alleviating the symptoms of a disorder resulting from a disease or a dysfunction of human or animal body or to heal it” (*Cour d’Appel* of Paris, 4th ch., 29 October 1997 *PIBD* 1998, No. 646, III, 29). And the EPO Boards of Appeal have defined the term “medical treatment” as “any non-insignificant intentional physical or psychic intervention performed directly or indirectly by one human being – who need not necessarily be a medical practitioner – on another (or, by analogy, on animals) using means or methods of medical science” (Tech. Board of Appeal EPO, 30 July 1993, T. 182/90, *OJ EPO* 1994, p. 641, pt 2.2).

Main claim 1 relating to a subject-matter excluded from patentability was then invalid. And the dependent claims 2 and 3 were also invalid since they were, in the same way, new only owing to the dosage taught.

The decision is also interesting as it specifies the authority that the French court is prepared to recognise to the EPO decisions or to the courts of other Member States of the European Union. After noting that these decisions have no legal binding force for national courts (the EPO is not a court so that its decisions even issued by the Enlarged Board of Appeal are merely indications of the analysis made by the EPO to grant European patents, and decisions of the courts of other Member States of the European Union are not binding on national case law, but contribute to the legal debate by explaining the reasoning of each national court on the point of law referred to them), the *Tribunal de Grande Instance* of Paris demonstrate, by way of example that it can, however, recognise to these decisions some intellectual authority. It thus includes in its own reasoning foreign decisions which convinced it because of the quality of their reasoning, as here the decision in which the German Federal Patent Court ruled that “to develop a specific therapeutic care plan for a patient which includes the prescription and the dosage of the medicaments is an essential part of the treating doctor’s activity. The determination of a dosage as an integral part of the therapeutic process is therefore removed from the patent protection”. In contrast, the Paris Court is clearly against the interpretation of Article 54 (4) EPC 2000 adopted by the EPO Enlarged Board of Appeal in its decision G2/08 of 19 February 2010: “Furthermore, Article 54 (4) EPC, which allows a same medicament to be patented for a second therapeutic effect, is totally silent on the possibility of patenting a certain dosage so that the Enlarged Board of Appeal’s

answer according to which “such patenting is also not excluded where a dosage regime is the only feature claimed which is not comprised in the state of the art”, cannot be inferred from the Convention but from an interpretation of what a dosage is, that is, a second therapeutic application, which plainly it is not”. The *Tribunal* was also aware of the judgments given in the United Kingdom and in Germany about the same patent EP 0 724 444 (the UK Court of Appeal (Civil Division) London, on 21 May 2008, Case No. [2008] EWCA Civ. 444, decided that a dosage regime was patentable and that, in this particular case, it was novel and non-obvious; and the German Federal Patent Court, *Bundespatentgericht*, on 26 June 2008, Ni 58/06 (EU), decided that a dosage regime was patentable but that it was lacking novelty in this particular situation) but gave them no binding force.

Original French decision.
English translation.

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