Federal Court of Appeal | Cour d'appel fédérale

Date: 20231109

Docket: A-131-22

Citation: 2023 FCA 220

CORAM: **LOCKE J.A.**
MACTAVISH J.A.
MONAGHAN J.A.

BETWEEN:

APOTEX INC.

Appellant

and

JANSSEN INC. AND ACTELION PHARMACEUTICALS LTD.

Respondents

Heard at Toronto, Ontario, on October 3, 2023.

Judgment delivered at Ottawa, Ontario, on November 9, 2023.

REASONS FOR JUDGMENT BY: LOCKE J.A.

CONCURRED IN BY: MACTAVISH J.A.
MONAGHAN J.A.

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REASONS FOR JUDGMENT

LOCKE J.A.

I. Overview

[1] This appeal concerns an allegation by the respondents, Janssen Inc. and Actelion Pharmaceuticals Ltd. (collectively, Janssen), that the marketing and sale by the appellant, Apotex Inc. (Apotex), of a pharmaceutical product called Apo-Macitentan would induce infringement of the respondents' Canadian Patent No. 2,659,770 (the Patent) by inducing physicians to prescribe

the drug to patients to be taken in combination with a phosphodiesterase type-5 inhibitor (PDE5 inhibitor) to treat a rare disease called pulmonary arterial hypertension (PAH). In an action pursuant to the *Patented Medicines (Notice of Compliance) Regulations*, S.O.R./93-133 (the *Regulations*), the Federal Court (2022 FC 996, *per* Justice Christine M. Pallotta) agreed with the respondents' allegation and enjoined Apotex from various activities involving Apo-Macitentan until the expiry of the Patent. Apotex appeals the Federal Court's decision.

[2] For the reasons set out below, I would dismiss the present appeal.

[3] The issue of inducing infringement is central in this case because the Patent is concerned with the treatment of vasoconstrictive diseases (such as PAH) by a combination of macitentan and a PDE5 inhibitor, whereas Apotex would sell macitentan alone. Apotex would not take part in the ultimate act of direct infringement by use of the patented combination.

II. Where the Parties Agree

[4] There is much on which the parties agree in this appeal. There is no argument that the Patent is invalid in any respect. The parties also agree that a party that does not directly infringe a patent may nevertheless be liable for patent infringement where it induces an act of direct infringement. They agree that the legal test for a finding of inducing infringement is as set out in *Corlac Inc. v. Weatherford Canada Ltd.*, 2011 FCA 228, 95 C.P.R. (4th) 101 at para. 162:

> It is settled law that one who induces or procures another to infringe a patent is guilty of infringement of the patent. A determination of inducement requires the application of a three-prong test. First, the act of infringement must have been completed by the direct infringer. Second, the completion of the acts of infringement

> must be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place. Third, the influence must knowingly be exercised by the inducer, that is, the inducer knows that this influence will result in the completion of the act of infringement: *Dableh v. Ontario Hydro*, [1996] 3 F.C. 751, paras. 42, 43 (C.A.), leave to appeal refused, [1996] S.C.C.A. No. 441; *AB Hassle v. Canada* (*Minister of National Health and Welfare*), 2002 FCA 421, 22 C.P.R. (4th) 1, para. 17 (C.A.), leave to appeal refused, [2002] S.C.C.A. No. 531; *MacLennan v. Les Produits Gilbert Inc.*, 2008 FCA 35, 67 C.P.R. (4th) 161, para. 13. The test is a difficult one to meet.

[5] The Federal Court correctly summarized the three prongs of this legal test at paragraph 147 of its reasons:

> 1. The acts of infringement must have been completed by the direct infringer;
>
> 2. The completion of the acts of infringement must be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place; and
>
> 3. The influence must be knowingly exercised by the inducer; in other words, the inducer knows that this influence will result in the completion of the acts of infringement.

[6] The parties also agree that the first prong of the test is met in this case. The dispute between the parties concerns the second and third prongs.

[7] Further, the parties agree, and I concur, that the standard of review to be applied by this Court is the normal appellate standard as set out in *Housen v. Nikolaisen*, 2002 SCC 33, [2002] 2 S.C.R 235. Questions of law are reviewed on a standard of correctness, and questions of fact or of mixed fact and law, from which no legal question is extricable, are reviewed on a standard of palpable and overriding error. A palpable error is one that is obvious. An overriding error is one that goes to the very core of the outcome of the case. It is not enough to pull at leaves and branches and leave the tree standing. The entire tree must fall: *Benhaim v. St-Germain*, 2016 SCC 48,

[2016] 2 S.C.R. 352 at para. 38 (*Benhaim*), quoting from *Canada v. South Yukon Forest Corporation*, 2012 FCA 165, 431 N.R. 286 at para. 46. A palpable and overriding error is in the nature not of a needle in a haystack, but a beam in the eye: *Benhaim* at para. 39, quoting from *J.G. v. Nadeau*, 2016 QCCA 167, [2016] J.Q. no 635 (QL) at para. 77.

[8] It is also common ground between the parties that Apotex seeks marketing approval for Apo-Macitentan as a generic version of Janssen's previously approved macitentan product called Opsumit. The Patent is on the Patent Register contemplated in the *Regulations* associated with Opsumit such that Apotex was required to address the Patent before it could obtain marketing approval for its generic product.

[9] An important area of focus in this case is the product monograph (PM) related to Apo-Macitentan, which provides information to the public concerning the drug and its uses. The parties agree that a PM may be relevant on the question of whether the second prong of the test for inducing infringement is met, including with regard to the possible influence on prescribing physicians' decisions. However, the parties disagree on whether sufficient influence is present in this case.

III. Second Prong: Influence

[10] As indicated above, the second prong of the test for inducing patent infringement requires that the acts of direct infringement be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place.

[11] Apotex argues that this prong would not be met by its Apo-Macitentan product because it would be marketed for non-infringing monotherapy and not for the patented combination treatment. Though Apotex acknowledges that Apo-Macitentan would be prescribed for the patented combination treatment, it argues that such use would not be because of its influence. Though Janssen's Opsumit product is intended to be used in combination treatment, and its associated PM so indicates, Apotex argues that its own PM omits references to combination treatment.

[12] The Federal Court analyzed this issue at paragraphs 176 to 199 of its reasons. After discussing the relevant jurisprudence (on which the parties do not appear to disagree), the Federal Court made the following findings in arriving at its conclusion that the second prong of the test was met:

1. The standard of care for PAH patients is combination treatment, usually involving an endothelin receptor antagonist (ERA) like macitentan and a PDE5 inhibitor (paragraph 183 of the Federal Court's reasons);

2. More than a majority of PAH patients who are prescribed Opsumit also receive a PDE5 inhibitor in combination (paragraph 183 of the Federal Court's reasons);

3. Few physicians are permitted to prescribe macitentan, and any who do would be aware of data related to a landmark clinical study known as SERAPHIN, which showed that combination treatment of macitentan and a PDE5 inhibitor was safe and

effective, as was treatment with macitentan alone (paragraphs 184 to 187 of the Federal Court's reasons);

4. Though the PM for Apo-Macitentan omits explicit references to combination treatment that are found in the PM for Opsumit, the evidence did not support a finding that doctors would carry out a side-by-side comparison of PMs. A significant portion of the information in the Apo-Macitentan PM is clinical trial data from the SERAPHIN study. The Apo-Macitentan PM, read as a whole, does not suggest that physicians should depart from well-established prescribing practices, principally combination treatment (paragraphs 188 to 193 of the Federal Court's reasons); and

5. Physicians treating PAH will review and rely on the Apo-Macitentan PM when prescribing treatment (paragraphs 195 to 198 of the Federal Court's reasons).

[13] An oft-quoted statement on the relevance of a PM to the issue of inducement is found in *Novopharm Limited v. Sanofi-Aventis Canada Inc.*, 2007 FCA 167, 366 N.R. 231 at para. 11 (*Novopharm*):

> A generic drug manufacturer may be implicated in the infringement by others of a claim for a new use of a medicine if the generic drug manufacturer induces that infringement. Infringement by inducement may be established, for example, by inferences reasonably drawn from the contents of the product monograph for the generic drug product, or evidence relating to the dosage form of the generic product, or its labelling or marketing. However, an inducement to infringe generally cannot be inferred from a mere reference to the new use in the product monograph, for example, in the course of explaining contraindications or drug interactions, or as part of a list of scientific references.

[14] This passage, which was recently quoted in *Teva Canada Limited v. Janssen Inc.*, 2023 FCA 68 at para. 106, was considered at paragraph 163 of the Federal Court's reasons in

this case. No inducement was found in *Novopharm*. However, *Novopharm* is distinguishable from this case in that the previous approval of the drug in question there (Ramipril) was for an entirely different and non-infringing use: treating hypertension rather than the patented use (treatment of schizophrenia and related disorders, which remained off-label). Here, the difference between the infringing use and the non-infringing use is far less significant. Apotex seeks approval, based on marketing approval previously granted for Opsumit, to use macitentan to treat certain classes of PAH, which is the same indication as contemplated in the Patent. The distinction Apotex relies on is that Apo-Macitentan is to be used alone rather than in combination with a PDE5 inhibitor, as contemplated in the PM for Opsumit.

[15] Inducement has been found based on a PM: e.g. *Genpharm Inc. v. AB Hassle*, 2004 FCA 413, 329 N.R. 374, and *Abbott Laboratories Limited. v. Canada (Ministry of National Health and Welfare)*, 2006 FC 1411, 55 C.P.R. (4th) 48, affirmed 2007 FCA 251, [2007] F.C.J. No. 935 (QL). The latter case, as here, involved an effort to cleanse a PM of references to a patented use.

[16] Apotex argues that the Federal Court erred in finding that the Apo-Macitentan PM could be the source of influence sufficient to satisfy the second prong of the test for inducing patent infringement. It relies on two facts to support its argument:

1. The Indications and Clinical Use section of the Apo-Macitentan PM does not mention combination treatment, such that Apotex would not be allowed to market Apo-Macitentan for use in combination with a PDE5 inhibitor; and

2. The Apo-Macitentan PM omits mention of scientific data that suggests the use of macitentan in combination with other drugs, such that "it is not reasonable to assume that the [Apo-Macitentan] PM intended to suggest that [Apo-Macitentan] could be used in a manner that departs from that for which is it is indicated – i.e. the treatment of PAH *as a monotherapy*." (italics in original) (see paragraph 42 of Apotex's factum)

[17] The weakness of Apotex's position in this regard is that it assumes that an absence of explicit instruction and of intention that direct infringement should result equals an absence of influence sufficient to satisfy the second prong. That is not necessarily the case. While explicit instruction and intention may be relevant to the issue of influence, I do not accept that either is required. Even without explicit reference to combination treatment, the Federal Court was entitled to find that the Apo-Macitentan PM would influence use of macitentan in that way.

[18] In my view, the Federal Court made no error of law regarding the second prong of the test for inducing infringement. Moreover, though the Federal Court's analysis as to how it concluded that the PM would have sufficient influence to satisfy the second prong could have been more fulsome, I am not convinced that the Federal Court made any palpable and overriding error in its consideration and application of the evidence. The Federal Court was clearly convinced that the PM would influence physicians to prescribe combination treatment, even though it does not explicitly mention such treatment. Moreover, because the Federal Court clearly understood the legal test, I infer that it was also convinced that the influence of the PM

was sufficient that, without it, direct infringement would not occur. In my view, these conclusions were available to the Federal Court.

IV. Third Prong: Knowledge

[19] The third prong of the test for inducing patent infringement, as discussed above, requires that the inducer know that their influence will result in the completion of the acts of infringement. The parties agree that this prong refers to knowledge that the influence is being exercised, rather than knowledge that the resulting activity will be an infringement: *Hospira Healthcare Corporation v. Kennedy Trust for Rheumatology Research*, 2020 FCA 30, 316 A.C.W.S. (3d) 537 at para. 45.

[20] Here, Apotex relies on an absence of evidence that it knew that physicians would be influenced by the Apo-Macitentan PM to prescribe the drug in a way that infringes the Patent. Without such evidence, Apotex argues, there was no basis for the Federal Court's finding that the third prong was met.

[21] The Federal Court found that Apotex knew or should have known that its PM would influence physicians' prescribing decisions. This conclusion appears to be based on evidence considered in relation to the second prong.

[22] Apotex argues that the Federal Court:

1. Conflated the second and third prongs of the test for inducing infringement;

2. Improperly shifted the burden of proof to Apotex;

3. Erred by failing to give sufficient weight to the evidence of Apotex's expert witness Ms. Picard; and

4. Erred in finding that there was no evidence from Apotex as to its knowledge of influence, and in overlooking evidence, including that Apotex does not intend to advise third parties as to the use of Apo-Macitentan.

[23] I find no merit in any of these arguments. I do not agree that the Federal Court conflated the second and third prongs of the test for inducing infringement, nor that it shifted the burden of proof. Moreover, it was open to the Federal Court to weigh Ms. Picard's evidence as it did, and it is not the role of this Court to reweigh this evidence in the context of this appeal. Finally, the Federal Court did not find, as Apotex argues, that "there was no evidence from Apotex as to its knowledge." (see paragraph 76 of Apotex's factum) Rather, the Federal Court stated at paragraph 203 of its reasons that "there is no evidence before the Court about Apotex's efforts to remove information from the PM." That statement does not appear to be wrong.

[24] The Federal Court was entitled to draw inferences about Apotex's knowledge from the evidence before it. Clearly, Apotex was aware of the content of the Apo-Macitentan PM, and the fact that it would be available to physicians treating PAH. Based on the evidence, it was open to the Federal Court to conclude that Apotex knew or should have known that the Apo-Macitentan PM would influence physicians' prescribing decisions.

V. Conclusion

[25] I would dismiss this appeal with costs to the respondents in the agreed-upon amount of $10,000.

[26] In closing, I take this opportunity to thank the parties for their very able submissions and for their work to trim the issues in dispute. This has not only assisted the Court in releasing a decision in this appeal with a minimum of delay, but I believe it has benefited the parties by focussing on the issues most likely to affect the outcome.

"George R. Locke"
J.A.

"I agree
Anne L. Mactavish J.A."

"I agree
K.A. Siobhan Monaghan J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

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