C A N A D A

PROVINCE OF QUÉBEC
DISTRICT OF MONTREAL

Nº: 500-06-000648-135

SUPERIOR COURT
(Class Action Division)

CAMILO BARATTO

Plaintiff

v.

MERCK CANADA INC.

MERCK FROSST CANADA & CO

Defendants

APPLICATION TO STRIKE
IMMATERIAL ALLEGATIONS AND EXHIBITS

(Art. 169 C.C.P.)

TO THE HONOURABLE CHRISTINE BAUDOUIN, J.S.C., SITTING AS CASE MANAGEMENT JUDGE IN THE PRESENT ACTION, THE DEFENDANTS SUBMIT THE FOLLOWING:

I. INTRODUCTION

1. On July 17, 2019, the Plaintiff filed his Originating Application herein, as appears from the Court record.

2. The Plaintiff essentially alleges that the Defendants ("**Merck**") failed to disclose the purported risk of persistent sexual side effects caused by the consumption of Propecia and Proscar, whose active ingredient is finasteride, to class members.

3. The Originating Application includes exhibits composed of purportedly "scientific" studies, commentaries, literature reviews and meta-analyses, all of which advance various opinions and hypotheses: Exhibits P-3A to P-3D, P-7A to P-7G, P-8 and P-9.

4. Merck is well founded in fact and in law to demand that this Court strike from the record (i) paragraphs 3.16 and 4.7 of the Originating Application as they contain immaterial allegations, and (ii) the impugned exhibits as they are inadmissible and

their inclusion in the Originating Application prejudices Merck's ability to fairly and effectively defend itself against the Plaintiff's allegations, as more fully detailed below.

II. PARAGRAPHS 3.16 AND 4.7 OF THE ORIGINATING APPLICATION

5. Paragraph 3.16 of the Originating Application lists the side effects that are infrequently reported for Propecia as disclosed in the product monograph dated October 1, 2018, and gratuitously mentions that the reported side effects in the 2018 product monograph are more numerous than those reported during the relevant class period.

6. It is normal and expected for post-marketing adverse drug reaction data — which is unsolicited, unverified and does not allow for conclusions regarding causality to be drawn — to be reported over time as a drug becomes more widely used.

7. The Plaintiff alleges that specific persistent side effects are caused by finasteride. The Court of Appeal authorized the class action accordingly, for a specific period of time.

8. That the reported side effects of finasteride are more numerous now than they were during the relevant class period and now include side effects which were never alleged by the Plaintiff has no relevance to his cause of action.

9. Similarly, paragraph 4.7 of the Originating Application alleges that the November 2011 versions of the product monographs for Propecia and Proscar minimize the risks associated with those medications.

10. The end of the relevant class period, November 18, 2011, coincides with the date Merck updated the product monographs in question.

11. The question that this Court needs to answer is whether the product monographs issued by Merck prior to November 2011 contained sufficient disclosures about the risks associated with finasteride, as of the information available on that date.

12. Whether the November 2011 product monographs themselves contain sufficient disclosures about the risks associated with finasteride is thus completely outside the scope of the common issues authorized by the Court of Appeal.

13. Paragraphs 3.16 and 4.7 are immaterial to any of the authorized common issues and must be struck from the Originating Application.

III. EXHIBITS

A. Generally

14. The present proceedings are no longer at the authorization stage. The Plaintiff now has the burden of proving his cause of action on the balance of probabilities according to the ordinary rules of evidence and Merck has the right to know the exact allegations against which it must defend itself and the evidence on which those allegations are based.

15. It would be unfair to require Merck to mobilize its resources in order to counter or explain each of the impugned exhibits. The impugned exhibits constitute inadmissible opinion and hearsay evidence, are irrelevant and unreliable and therefore are of no assistance to the Court in its role as trier of fact.

16. The impugned exhibits advance opinions and hypotheses that were not properly introduced into evidence by means of an expert report. The authors of the impugned exhibits were not sworn in and did not sign a declaration regarding the carrying out of their mission as an expert tasked with enlightening the Court in making its decision.

17. Opinions that are not put forward in an expert report in accordance with the case protocol are inadmissible.

18. Accordingly, the impugned exhibits must be struck on this basis alone.

19. The impugned exhibits are also replete with out-of-court statements that are tendered for the truth of their contents and that are not subject to contemporaneous cross-examination. Merck is unable to question their authors regarding the methods they used, the assumptions they made, the hypotheses they were testing or advancing, their sources of funding or affiliations, and their interpretation of the results they obtained.

20. The impugned exhibits clearly constitute inadmissible hearsay evidence in their face, and must be struck.

B. None of the Articles Filed Suggest or Purport to Suggest that Finasteride Causes Persistent Sexual Side Effects

1) One Analysis of Prepuce Specimens that Contradicts the Plaintiff's Claim

21. Exhibit P-3C: C. Di Loreto *et al*., *Immunohistochemical Evaluation of Androgen Receptor and Nerve Structure Density in Human Prepuce from Patients with Persistent Sexual Side Effects after Finasteride Use for Androgenetic Alopecia* (2014)

a) This study analyzed androgen receptor and nerve density in prepuce specimens of eight men who reported persistent sexual side effects after having discontinued finasteride.

b) The purpose was to investigate whether these side effects resulted from a deficiency of androgen receptor cells in the prepuce.

c) However, the "unexpected result" of the study is that there was a significant increase of androgen receptor cells in the participants' prepuce samples.

d) The authors have no choice but to conclude that their data exclude the impairment they hypothesized in the prepuce.

e) Aside from this result, the study's sample of eight men is exceedingly small, and was also afflicted with clear selection bias as three (38%) were recruited from the anti-finasteride website "propeciahelp.com". Moreover, all purported sexual side-effects were self-reported, with no actual diagnosis.

f) The study's limitations preclude it from supporting the proposition that finasteride causes persistent sexual side effects, in fact its results contradict the hypothesis posited by the authors.

2) One Irrelevant Prospective Study Regarding Depressive Symptoms

22. Exhibit P-7E: B. Rahimi-Ardabili et al., Finasteride induced depression: a prospective study (2006)

a) This study examines whether depressive symptoms or anxiety might be induced by finasteride use after two months of beginning treatment. It found a "minimal, but statistically significant" increase in the reporting of depressive symptoms during treatment.

b) Limitations of this study include lack of a control group and short period of observation. The study therefore does not support a causal association between therapy with finasteride and the development of depressive symptoms or anxiety symptoms in patients taking finasteride.

c) Moreover, this study is irrelevant on its face as it only examined depressive symptoms that manifested during finasteride use, not after discontinuation of treatment.

d) Nothing in this study suggests or purports to suggest that finasteride causes persistent side effects.

3) Three Irrelevant Surveys of Self-Diagnosed Men, Which Do Not Suggest Nor Purport to Suggest that Finasteride Causes Persistent Sexual Side Effects

23. Exhibit P-7B: M.S. Irwig *et al*., Persistent *Sexual Side Effects of Finasteride for Male Pattern Hair Loss* (2011)

a) This survey in which the authors conducted interviews with men who reported persistent sexual side effects and was carried out to determine the types and duration of persistent sexual side effects associated with finasteride use — not to investigate whether finasteride can cause any such side effects.

b) This study suffers from several methodological limitations.

c) The first limitation is the absence of any control group with which to compare the men who had used finasteride.

d) A second limitation is that the sample of participants is afflicted with selection bias due to the fact that study participants were recruited through word of mouth and from the anti-finasteride website “propeciahelp.com”.

e) A third limitation is recall bias since the participants’ symptoms were self-reported with no actual diagnosis on average 40 months after discontinuing finasteride before they were interviewed.

f) The authors acknowledge that the study “does not prove that finasteride caused persistent sexual side effects”, and add:

> Our study has several limitations. Most importantly, the retrospective nature of this study does not allow us to estimate what percentage of prospective finasteride users would develop persistent sexual side effects. A second limitation is selection bias in which those subjects experiencing more severe side effects, or those for whom sexuality is a more significant aspect of their life, would be more likely to participate in a study looking at sexual parameter. Another limitation is recall bias, in which subject may not have remembered certain details such as the exact month when they started finasteride. Furthermore, no serum hormone levels were measured.
>
> [Our emphasis.]

g) Because of its design and unsound methodology, this study does not support the proposition that men who use finasteride for treatment of male pattern hair loss are at increased risk of persistent sexual dysfunction.

24. Exhibit P-7C: M.S. Irwig, *Persistent Sexual Side Effects of Finasteride: Could They Be Permanent?* (2012)

a) Exhibit P-7C is an abstract of a follow-up of the previous study (Exhibit P-7B). It is thus inherently affected by the same limitations.

25. Exhibit P-7F: C.A. Ganzer et *al*., *Persistent Sexual, Emotional, and Cognitive Impairment Post-Finasteride: A Survey of Men Reporting Symptoms* (2014)

a) This web-based survey consists in asking former finasteride users who self-identify as having “post-finasteride syndrome” to report symptoms that “they believed” were associated with finasteride use.

b) It does not purport to investigate any causal relationship between finasteride use and persistent sexual side effects.

c) This study also suffers from a number of limitations.

d) First, there was no control group for comparison.

e) Second, the authors did not use a validated instrument to measure psychological and cognitive effects since the authors created their own web survey.

f) Third, the sample of participants is afflicted with selection bias as they were recruited from the anti-finasteride website “propeciahelp.com”.

g) Fourth, the use of retrospective (*i.e.,* survey) methodology introduces recall bias.

h) Additionally, this study is also not reliable evidence of persistent sexual dysfunction because 84% of the study subjects reported that they had no symptoms while taking the medication but that symptom onset began **after** discontinuing the medication.

i) This study does not support the proposition that finasteride causes persistent side effects.

4) <u>Two Irrelevant “Commentaries” that Prove Nothing but the Opinions of their Authors</u>

26. Exhibit P-3A: S. Frankel, *Study of the Food and Drug Administration Files on Propecia* (1999)

a) This is a commentary by a professor of physics (not a medical doctor) who conveys his opinions regarding the approval of Propecia by the FDA.

b) It is an opinion piece and its sole references consist of six articles of which he was the sole author.

c) The author merely provides a commentary on the generalizability of certain prior studies, and asks whether the 1 mg dose of finasteride approved by the FDA (and, incidentally, all other countries where finasteride is prescribed to treat alopecia) is excessive.

d) The author does not purport to offer any evidence as to any persistent sexual side effects caused by finasteride. In fact, nothing in this article suggests or purports to suggest that finasteride causes persistent side effects.

e) Exhibit P-3A is a piece of pure commentary that is irrelevant to the Plaintiff's cause of action.

5) Exhibit P-9: I. Goldstein, An Old Problem with a New Cause – 5 Alpha Reductase Inhibitors and Persistent Sexual Dysfunction (2011)

f) This editorial is nothing but a pure, unadulterated opinion piece on the part of its author.

g) It is essentially based on anecdotal evidence and the flawed articles by Traish *et al.* (Exhibit P-7A) and Irwig *et al.* (Exhibit P-7B) discussed above and below.[1]

h) This commentary proves nothing but the personal opinion of its author and must be struck from the record.

[1] The third study cited at footnote 12 of Exhibit P-9 does not examine persistent sexual side effects.

6) Four Literature Reviews that Do Not Show Nor Purport to Show Causation Between Finasteride Use and Persistent Side Effects

27. Exhibit P-7A: A.M. Traish *et al.*, *Adverse Side Effects of 5α-Reductase Inhibitors Therapy: Persistent Diminished Libido and Erectile Dysfunction and Depression in a Subset of Patients* (2011)

a) This review article is speculative in nature and consists in a literature review of prior papers respecting side effects of finasteride and dutasteride.

b) The author speculates on the "possibility" of a causal relationship between finasteride use and persistent sexual side effects.

28. Exhibit P-7D: A.M. Traish *et al*., *Adverse effects of 5α-reductase inhibitors: What do we know, don't know, and need to know?* (2015)

a) Most of the issues discussed in this literature review (such as those relating to the effects of 5α-RI therapy on insulin resistance or bone metabolism) are irrelevant.

b) The only discussion of finasteride-induced persistent sexual side effects is confined to a single paragraph and, according to the authors, the reviewed studies raise "a number of methodological concerns due to recall and selection bias, as well as lack of placebo-treated controls".

c) Moreover, these studies are already included by the Plaintiff as Exhibits P-3B, P-7A and P-7B. The Plaintiff is thus using P-7D as an echo chamber so that he can get additional mileage from his other exhibits.

d) The author himself acknowledges that "the persistence of such side effects, if confirmed, remains poorly understood and controversial." (we underline).

29. Exhibit P-7G: A.M. Traish, *The Post-finasteride Syndrome: Clinical Manifestation of Drug* Induced *Epigenetics Due to Endocrine Disruption* (2018)

a) In this review article, the author speculates on possible mechanisms for finasteride to induce alleged persistent sexual side effects.

b) The author's "hypothetical model of finasteride acting as an endocrine disrupter" is not based on reliable scientific data and is pure speculation on his part.

c) The author confirms he received fees from Johnson and Becker, a plaintiff's class action law firm involved in litigation against Merck affiliates in the United States (p. 98), then basically argues for the recognition of a so-called "post-finasteride syndrome."

30. Exhibit P-8: *QuarterWatch: Finasteride (PROPECIA, PROSCAR receptor) and possibly persistent sexual side* effects (2013)

a) This report seeks to determine if there exists a "signal" for persistent sexual side effects in FDA post-marketing reports of users for the second quarter of 2012.

b) It does <u>not</u> purport to describe any causal relationship between finasteride use and persistent sexual side effects. In fact, this type of voluntary post-marketing data cannot provide reliable scientific evidence demonstrating that Propecia is significantly associated with or causes persistent side effects following drug discontinuation. Voluntary reporting of adverse events can suffer from notoriety bias (a form of selection bias) due to selective reporting by patients, physicians, and other health care providers. This form of bias is likely for an outcome that is largely based upon self-report, such as sexual dysfunction, because of digital media reports and the nocebo effect.

c) It indicates, among other things, that awareness of the supposed risk of finasteride-induced persistent sexual side effects was only "emerging" in 2013, that is, long after Merck had already updated its product monograph and outside the relevant period for the present class action.

7) <u>Two Meta-Analyses</u>

31. Exhibits P-3B and P-3D are meta-analyses, that is, statistical analyses that combine the results of several studies.

32. Exhibit P-3B: S. M. Belknap *et al*., *Adverse Event Reporting in Clinical Trials of Finasteride for Androgenic Alopecia – A Meta-analysis* (2015)

    a) This article claims to be a meta-analysis of adverse event *reporting i*n 34 clinical trials assessing finasteride for the treatment of alopecia.

    b) This article has nothing to do with persistent sexual dysfunction since it merely evaluated on-drug adverse event reporting in finasteride clinical trials for male pattern hair loss.

    c) While the authors, financed in part by the "Post-Finasteride Syndrome Foundation", criticize the methodology used in these trials, nowhere do they indicate <u>any</u> support for a causal relationship between finasteride use and purported persistent sexual side effects.

33. Exhibit P-3D: T. Kiguradze *et al.*, *Persistence of Sexual Dysfunction in Young Men Receiving Finasteride for Androgenic Alopecia: A Large Single Center Observational Cohort Study* (undated)

    a) The authors ran a statistical analysis on an electronic medical record database in order to identify healthy men who developed persistent sexual side effects after taking 5a-reductase inhibitors, including finasteride. do not support the proposition that Propecia causes persistent sexual dysfunction.

    b) The analysis in Exhibit P-3D identified 47 or 1.1% of the 4,274 men sampled as having developed persistent sexual side effects following finasteride use. No control group is identified, it is unknown whether the 47 individuals were actually diagnosed with any form of persistent sexual side effects, and whether they suffered from sexual dysfunction prior to finasteride use.

    c) This Exhibit shares many of the same authors as Exhibit P-3B, which was funded by the "Post-Finasteride Syndrome Foundation" website.

34. This Application to Strike Immaterial Allegations and Exhibits is well founded in fact and in law.

FOR THESE REASONS, MAY IT PLEASE THE COURT:

TO GRANT the Defendants' Application to Strike Immaterial Allegations and Exhibits;

TO STRIKE paragraphs 3.16 and 4.7 from the Plaintiff's Originating Application;

TO STRIKE Exhibits P-3A, P-3B, P-3C, P-3D, P-7A, P-7B, P-7C, P-7D, P-7E, P-7F, P-7G, P-8 and P-9 from the Court record and all references thereto from the Plaintiff's Originating Application;

THE WHOLE with costs.

Montréal, November 20, 2020

Blake, Cassels & Graydon L.L.P.

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NOTICE OF PRESENTATION

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TAKE NOTICE that the present *Application to Strike Immaterial Allegations and Exhibits* will be presented for adjudication before the honourable Christine Baudouin, J.S.C. of the Superior Court of Québec, sitting in the Class Action Division for the District of Montreal, on **December 8, 2020**, at **2:00 PM**, in room to be determined, at the Montreal Courthouse located at 1, Notre-Dame Street East, Montréal, Québec, H2Y 1B6.

DO GOVERN YOURSELVES ACCORDINGLY.

Montréal, November 20, 2020

Blake, Cassels & Graydon L.L.P.

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(ART. 169 C.C.P.)

ORIGINAL

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