Litigation associated with 5-alpha-reductase-inhibitor use: A Canadian legal database review

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Introduction: *5α-reductase inhibitors (5ARI) are commonly prescribed medications. There is ongoing controversy about the adverse events of these medications. The aim of this study is to characterize lawsuits in Canada involving medical complications of 5ARIs use.*

Materials and methods: *Legal cases were queried from CanLII. Cases were included if they involved a party taking a 5ARI who alleged an adverse event. Relevant full cases were retained, and pertinent characteristics were extracted with the help of a legal expert.*

Results: *Our deduplicated search yielded 67 unique legal documents from December 2013 to February 2019. Twelve of these documents met the inclusion criteria (representing 3 cases, considering each case had several hearings). The medical complaints filed by the plaintiffs were all related to medication side effects (n = 3, 100%). The plaintiffs were commonly patients themselves. Defendants were exclusively pharmaceutical companies. Persistent erectile dysfunction after stopping the medication was cited as a side effect in all complaints. The prescriptions were made for male pattern hair loss (n = 3, 100%) in all cases. All cases represent class actions brought by the plaintiffs, and they have been certified by their respective court. However, the cases are still ongoing.*

Conclusion: *While 5ARI use has been linked to undesired sexual side effects, there have been few litigations on this issue in Canada. Persisting sexual dysfunction after stopping the medication is the only complaint presented in legal action. To date, no judgment against a physician or pharmaceutical company was identified. Cases are still ongoing.*

Key Words: 5α-reductase inhibitors, adverse events, side effects, lawsuits, complications, legal, complaints, sexual dysfunction

Introduction

There is ongoing controversy regarding the adverse events associated with 5-alpha-reductase inhibitors (5ARI) which are indicated for the management of benign prostatic hyperplasia (BPH) and androgenetic alopecia. The known side effects of this medication include decreased libido, erectile dysfunction, and ejaculatory dysfunction. In addition to those well-established side effects, more controversial reports of persistent sexual dysfunction after discontinuation, depression, and suicidality have emerged, primarily for finasteride.[1-7] These concerns have resulted in the recent coining of the Post-Finasteride Syndrome and the creation of patient advocacy groups such as the Post-Finasteride Syndrome Foundation in 2012.

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Lawsuits may be the result of adverse outcomes associated with 5ARI use. Low et al characterized 18 lawsuits in the United States involving the adverse side effects of 5ARI and found that 5ARI was alleged to have sexual, mental, and physical side effects, resulting in legal disputes.[8] They also noted an increase in the number of lawsuits since 2018, suggesting that litigation around 5ARI will be an integral part of the US medical malpractice landscape for many years to come.

As there is currently no literature reporting the medicolegal landscape of 5ARI prescription in Canada, we sought to conduct a legal database review of litigation from adverse events associated with 5ARI use in Canada. The aim of this analysis is to characterize lawsuits involving the adverse side effects of 5ARI to better understand the drivers of litigation.

Materials and methods

Case identification

We conducted a search of the Canadian Legal Information Institute (CanLII) database in June 2022 from inception to May 2022. CanLII provides access to court judgments from all Canadian courts, including the Supreme Court of Canada, federal courts, and courts in all of Canada's provinces and territories. This reference is publicly available. Additional information can be found at https://www.canlii.org/en/info/about.html.

The search strategy was based on the study by Low et al.[8] Search terms included "5-alpha reductase inhibitor", "finasteride," "dutasteride," "Propecia," "Proscar," or "Avodart," in combination with "malpractice," "negligence," "damage," "loss," "side effect," "tort," "standard of care," "injury," and "complication."

Cases were included if the basis of the litigation was alleged adverse events secondary to 5ARI use. Excluded cases represented documents that were either unrelated to 5ARI, erroneous capture or product liability that did not have a medical allegation. Two reviewers independently screened each title and case summary in the first round of reviews following the inclusion and exclusion criteria. Full case texts were reviewed in the second round. Conflicts were resolved by a third reviewer.

Data collection and analysis

Pertinent characteristics of retained cases (province, court, year of certification/authorization, plaintiff, defendant, reason for prescription, reasons alleged for class-action lawsuit, outcomes) were extracted with the help of a legal researcher.

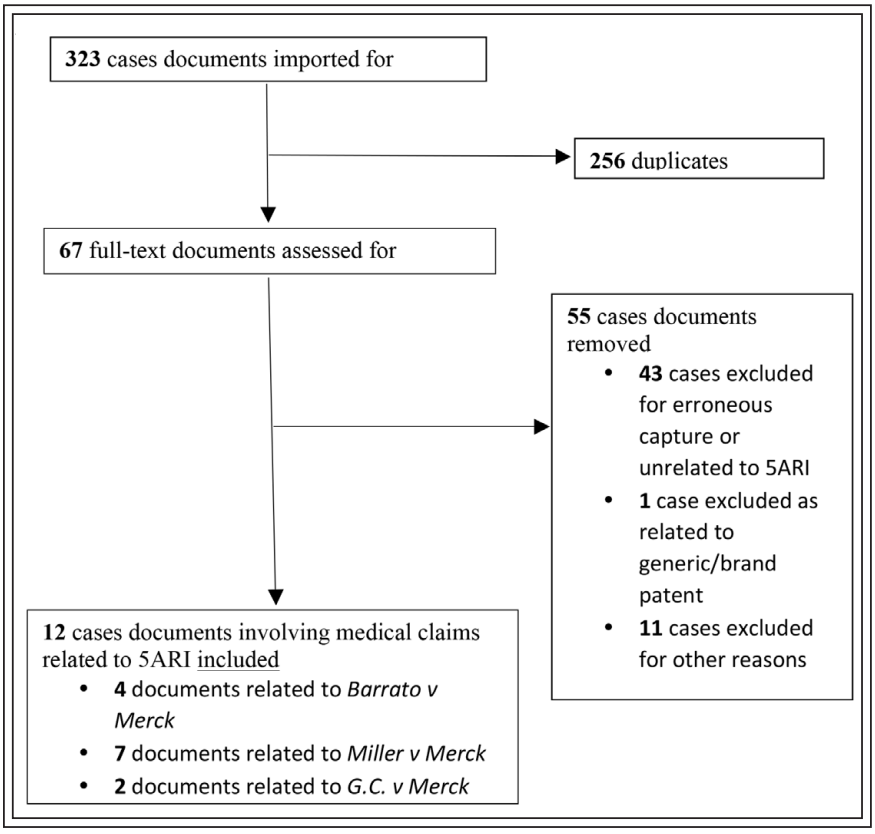

Figure 1. Case inclusion criteria.

Results

Search results

Our deduplicated search yielded 67 unique case documents ranging from December 2013 to February 2019. Cases involving medical claims related to 5ARI were included. Twelve of these documents met the inclusion criteria (representing 3 cases, considering each case had several hearings). Excluded cases included those unrelated to 5ARI, or those concerned with generic versus brand patent. Some cases were excluded for other reasons. For example, cases where patients were attempting to sue the clinician for practice negligence (but not directed against 5ARI particularly). Case identification is depicted in Figure 1.

Case characteristics

The medical complaints filed by the plaintiffs were all related to medication side effects (n = 3, 100%). The plaintiffs were commonly patients themselves. Defendants were exclusively pharmaceutical companies (n = 3, 100%; Merck was the defendant in all cases). Persistent erectile dysfunction after stopping the medication was cited as a side effect in all complaints. Erectile dysfunction is defined as the inability to have or maintain an erection for the purpose of a satisfying

TABLE 1. **Summary of cases**

Case **Province**	**Miller v Merck** **British Columbia**	**Baratto v Merck** **Quebec**	**G. C. v Merck** **Saskatchewan**
Year of certification (common law provinces) or authorization (QC) of class action	2013	2018	2019
Identified class of persons included in class action (plaintiffs)	"All male persons who were prescribed Propecia and/or Proscar for male pattern hair loss in British Columbia prior to November 18, 2011"	"All persons residing in Quebec who were prescribed the drugs Propecia and/or Proscar for the treatment of common baldness before November 18, 2011, and who developed at least one of the following conditions, which persisted following the cessation of Usage: Sexual dysfunction; Low libido; erectile dysfunction; Ejaculatory disorders; Reduced volume of ejaculate; Shrinkage of the genitals; Gynecomastia; Pain in the testicles; Anhedonia and difficulty reaching an orgasm, or; A Depression."	"All male persons who were prescribed Propecia or Proscar for male pattern hair loss or benign prostate hyperplasia in Canada prior to November 18, 2011."
Defendant	Pharmaceutical company, Merck	Pharmaceutical company, Merck	Pharmaceutical company, Merck
Reason for prescription of finasteride to representative plaintiff or identified class of plaintiffs	Male pattern hair loss	Male pattern hair loss	Male pattern hair loss
Alleged injuries to identified class of persons included in class action	Persistent sexual dysfunction following administration of finasteride and a failure on the part of the defendant to adequately warn of the potential side effects.	"Sexual dysfunction; Low libido; Erectile dysfunction; Ejaculatory disorders; Decreased volume of ejaculate; Shrinking of the genitals; Gynecomastia; Pain in the testicles; Anhedonia and difficulty reaching an orgasm, or Depression."	Persistent sexual dysfunction following administration of finasteride and a failure on the part of the defendant to adequately warn of the potential side effects.

sexual relationship. All prescriptions were made for the management of androgenetic alopecia (n = 3, 100%). Medication dosing included two prescriptions of Proscar 5 mg (pill divided into quarters) and 1 prescription of Propecia 1 mg. A summary of the facts in all 3 cases can be found in Table 1.

Legal analysis

All cases represent class actions filed in different Canadian provinces (British Columbia, Quebec and Saskatchewan) against the same pharmaceutical company. All three cases have been certified or granted authorization to proceed by courts, though this process was challenged in two cases. In Miller v. Merck, the defendant challenged the request for certification to the British Columbia Court of Appeal (BCCA).[9] Once certification was granted,[10] Merck appealed it both to the BCCA[11] and Supreme Court of Canada (SCC)[12] but was unsuccessful. In Baratto v. Merck, class action authorization was not granted at trial,[13] but succeeded on appeal.[14] The defendant appealed this decision to the SCC but was unsuccessful.[15] In G.C. v. Merck, class action certification was granted in first instance.[16] The fact that these different class actions have been challenged explains why we have identified 12 documents. As the class actions are still in progress, no decisions on the facts of each case have been rendered, and no verdicts have been made against physicians.

Discussion

Considering the ongoing controversy associated with adverse events of 5ARI and the lack of Canadian medico-legal analysis on this issue, we conducted a legal database review of CanLII. We only identified 3 cases in Canada, all occurring after 2012. All cases alleged persistent sexual dysfunction after stopping finasteride used for the management of androgenetic alopecia. None of the cases involved a physician. To compare, the study conducted in the United States reported 5 out of 18 lawsuits against physicians, of which 4 were against urologists. Other adverse events such as delayed cancer diagnosis and lack of symptom improvement were also causes for litigation in the US.

While no judgment has been made for any of the identified Canadian cases on 5ARI litigation, all cases are ongoing, and courts have affirmed certification or authorization at appeal in two cases. Thus, Canadian courts deem that these lawsuits have justifiable causes of action, identifiable classes of plaintiffs, and issues common to all plaintiffs to the extent that a class action lawsuit is warranted. Regardless of the final outcome of these cases, they act as a reminder to ensure that shared and informed decision-making occurs between the provider and their patient when prescribing drugs such as finasteride.

Persistent sexual dysfunction after finasteride discontinuation is controversial. While it has been identified in pharmacovigilance analyses, these studies are inherently limited.[2,5,7,9] Similarly, randomized control trials (RCT) have known limitations in assessing rare and long term effects. The lack of data on persistence of sexual dysfunction following discontinuation in RCTs limits the ability for further analyses.[10] Unsealed internal documents by Merck, the pharmaceutical company that produces Proscar and Propecia, also revealed that the company was aware that persistent erectile dysfunction was a potential risk of finasteride following analyses of their own pharmacovigilance data.[9] These concerns were dismissed due to limitations of pharmacovigilance data. Despite these limitations, Merck opted to pursue pharmacovigilance surveillance of persistent sexual dysfunction.

The lack of litigation associated with dutasteride and litigation occurring exclusively after 2012 (with the first case dating to December 2013) reveals a similar pattern uncovered by previous analyses of our group suggesting that increased attention associated with finasteride, but not dutasteride, may be driving more recent reporting of adverse events with finasteride and subsequently, litigation associated with the drug.[1,6] All cases identified were also for prescriptions made for the management of androgenetic alopecia. This is again in keeping with our previous work suggesting that most of the association of finasteride with adverse sexual and psychological events is driven by patients using the drug for hair loss.[1,6] When taking into account all the subgroup analyses of these two previous studies (which additionally include age-stratified analyses and comparisons to other drugs with similar indications and/or mechanisms of action), reports of sexual dysfunction linked with finasteride may be confounded by indication and stimulated reporting. This stimulated reporting can be perceived as biasing findings, but may also represent an affirmation of lived experience resulting in more open disclosure and confidence to litigate.

To our knowledge, this is the first study of its kind investigating 5ARI-associated litigation in Canada. One of the limitations of our study is the small number of identifiable cases (n = 3). Indeed, this limits the conclusions that we can draw, especially towards physicians, considering that the 3 defendants are pharmaceutical companies. However, this is in line with the legal database review conducted in the United States that only identified 18 legal cases with the first case dating back to 2003. For various reasons,

American physicians are 5 times more likely to be sued.[11] Additionally, while understanding the underlying risk of ED is important when assessing adverse events, this is a limitation in post-trial studies and remains beyond the scope of our study. Finally, our review did not capture cases settled out of court which is an inherent limitation to all medico-legal analyses.

Disclosures

Dr. Bhojani, Dr. Zorn and Dr. Elterman are consultants for Boston Scientific, Olympus, and Procept Biorobotics. Dr. Trinh reported receiving honoraria from Astellas, Bayer, and Janssen, and grants from Pfizer. All other authors report no disclosures. □

References

1. Nguyen DD, Marchese M, Cone EB et al. Investigation of suicidality and psychological adverse events in patients treated with finasteride. *JAMA Dermatol* 2021;157(1):35-42.
2. Ali AK, Heran BS, Etminan M. Persistent sexual dysfunction and suicidal ideation in young men treated with low-dose finasteride: a pharmacovigilance study. *Pharmacotherapy* 2015;35(7):687-695.
3. Irwig MS. Finasteride and suicide: a postmarketing case series. *Dermatology* 2020;236(6):540-545.
4. Gormley GJ, Stoner E, Bruskewitz RC et al. The effect of finasteride in men with benign prostatic hyperplasia. *N Engl J Med* 1992;327(17):1185-1191.
5. Irwig MS, Kolukula S. Persistent sexual side effects of finasteride for male pattern hair loss. *J Sex Med* 2011;8(6):1747-1753.
6. Nguyen DD, Herzog P, Cone EB et al. Disproportional signal of sexual dysfunction reports associated with finasteride use in young men with androgenetic alopecia: A pharmacovigilance analysis of VigiBase. *J Am Acad Dermatol* 2023;88(1):179-181.
7. Guo M, Heran B, Flannigan R, Kezouh A, Etminan M. Persistent sexual dysfunction with finasteride 1 mg taken for hair loss. *Pharmacotherapy* 2016;36(11):1180-1184.
8. Low P, Li KD, Hakam N et al. 5-Alpha reductase inhibitor related litigation: A legal database review. *Andrology* 2022;10(3):470-476.
9. Irwig MS. How routine pharmacovigilance failed to identify finasteride's persistent sexual side effects. *Andrology* 2022;10(2):207-208.
10. Zhang JJ, Shi X, Wu T et al. Sexual, physical, and overall adverse effects in patients treated with 5α-reductase inhibitors: a systematic review and meta-analysis. *Asian J Androl* 2022;24(4):390-397.
11. Coyte PC, Dewees DN, Trebilcock MJ. Medical malpractice — The Canadian Experience. *N Engl J Med* 2010;324(2):89-93.
12. Merck Frosst Canada Ltd., et al. v. Michael Miller, 2016 CanLII 20439 (SCC), https://canlii.ca/t/gphkt, retrieved on 2023-05-17.
13. Baratto c. Merck Canada Inc., 2016 QCCS 6664 (CanLII), https://canlii.ca/t/gx06p, retrieved on 2023-05-17.
14. Baratto c. Merck Canada Inc., 2018 QCCA 1240 (CanLII), https://canlii.ca/t/ht7cq, retrieved on 2023-05-17.
15. Merck Canada Inc., et al. c. Camilo Baratto, 2019 CanLII 23875 (CSC), https://canlii.ca/t/hzd20, retrieved on 2023-05-17.
16. G.C. v Merck Canada Inc., 2019 SKQB 42 (CanLII), https://canlii.ca/t/hxmbj, retrieved on 2023-05-17.