

Summary Safety Review - Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-norepinephrine Reuptake Inhibitors (SNRIs) – Assessing the Potential Risk of Sexual Dysfunction despite Treatment Discontinuation

Product:

- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin-norepinephrine reuptake inhibitors (SNRIs)

Potential Safety Issue: Persistent, worsening or new symptoms of sexual problems (dysfunction) despite stopping treatment.

Key Messages

- **SSRIs and SNRIs are prescription drugs authorized for sale in Canada to treat depression. Certain SSRI and SNRI products are also authorized for use in other conditions such as anxiety disorders and pain.**
- **Health Canada reviewed the potential risk of persistent or worsening sexual dysfunction, as well as the appearance of new symptoms of sexual dysfunction after stopping SSRI or SNRI treatment. This safety review was triggered by information received from the European Medicines Agency's Pharmacovigilance Risk Assessment Committee.**
- **Health Canada's review could not confirm, nor rule out, a causal link between stopping SSRI or SNRI treatment and persistent sexual dysfunction. The review found rare cases of long lasting sexual symptoms persisting after stopping SSRI or SNRI treatment.**
- **Health Canada's review could not make conclusions about worsening or new symptoms of sexual dysfunction as the available studies were not designed to assess this.**
- **Health Canada will work with manufacturers to update the product safety information for all SSRIs and SNRIs to recommend that healthcare professionals inform patients about the potential risk of long lasting (possibly weeks to years) sexual dysfunction despite discontinuation of SSRIs or SNRIs.**

Overview

It is well known that continued treatment with SSRIs and SNRIs can cause sexual problems (dysfunction) such as low sexual desire, problems maintaining an erection, orgasm problems, genital or nipple numbness, etc.

Health Canada reviewed the potential risk of persistent or worsening sexual dysfunction, as well as the appearance of new symptoms of sexual dysfunction after stopping SSRI or SNRI treatment. The safety review was triggered by information received from the European Medicines Agency, which was contacted by a group of physicians and scientists concerned that stopping SSRI or SNRI treatment could result in persistent, worsening, or new symptoms of sexual dysfunction.

Use in Canada

- In Canada, SSRIs and SNRIs are prescription drugs authorized for treating depression with certain products also authorized for other conditions such as anxiety disorders and pain.
- SSRIs authorized for use in Canada include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vilazodone and vortioxetine.
- SNRIs authorized for use in Canada include desvenlafaxine, duloxetine, levomilnacipran and venlafaxine.
- Over 37 million SSRI and SNRI prescriptions were filled in Canada in 2019.

Safety Review Findings

- Health Canada reviewed information from published and unpublished population-based (epidemiologic) studies and case reports of individual patients. Information was obtained from searches of international databases of published literature, drug manufacturers, physicians concerned about this issue, as well as searches of the Canada Vigilance database^a.
- Epidemiologic studies reporting sexual dysfunction with SSRIs or SNRIs use were not specifically designed to assess a link between treatment discontinuation and persistent, worsening, or new symptoms of sexual dysfunction, so were not included because of concerns about the accuracy of their findings.
- Health Canada's review of case reports focused on the outcome of persistent sexual dysfunction. Existing assessment tools were not designed to assess the link between treatment discontinuation and changes in patient symptoms (such as worsening of existing symptoms, or the appearance of new symptoms of sexual dysfunction).
- Of the 58 case reports of sexual dysfunction, 43 cases (16 Canadian, 27 international) of persistent sexual dysfunction were considered possibly linked to previous use and discontinuation of SSRI or SNRI treatment. The remaining 15 cases could not be assessed because there was not enough information. In some of these case reports, symptoms lasted long after treatment discontinuation (weeks to years).

Conclusions and actions

- Health Canada's review could not confirm, nor rule out, a causal link between stopping SSRI or SNRI treatment and persistent sexual dysfunction.
- Health Canada's review could not make conclusions about worsening or new symptoms of sexual dysfunction as the studies were not designed to assess this.
- Health Canada will work with manufacturers to update the product safety information for all SSRIs and SNRIs to recommend that healthcare professionals inform patients about the potential risk of long lasting (possibly weeks to years) sexual symptoms persisting after stopping SSRI or SNRI treatment.
- A Health Product InfoWatch Label Update will also be published.
- Health Canada encourages consumers and healthcare professionals to report any side effects related to the use of SSRIs and SNRIs and other health products to the Canada Vigilance program.
- Health Canada will continue to monitor safety information involving SSRIs and SNRIs to identify and assess potential risks, as it does for all health products on the Canadian

market. Health Canada will take appropriate and timely action should new health risks be identified.

Additional information

The analysis that contributed to this safety review included scientific and medical literature, information provided by drug manufacturers and physicians concerned about the risk, and Canadian and international adverse reaction reports, and what is known about the use of SSRIs and SNRIs both in Canada and internationally.

For additional information, contact the Marketed Health Products Directorate.

- a) Canadian reports can be accessed through the Canada Vigilance Online Database.