## Medicines Adverse Reactions Committee

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|---|---|---|---|
| Meeting date | 11/06/2026 | Agenda item | 3.2.3 |
| Title | **Update on sexual dysfunction (post SSRI sexual dysfunction, PSSD) following discontinuation of serotonin reuptake inhibitors** | | |
| Submitted by | Medsafe Pharmacovigilance Team | Paper type | For advice |

| **Active ingredient** | **Product name** | **Sponsor** |
|---|---|---|
| Citalopram | **Celapram** | Viatris Limited |
| Citalopram | Cipramil | Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics |
| Escitalopram | **Ipca-escitalopram** | Ipca Pharma (NZ) Pty Limited |
| Escitalopram | Lexapro | Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics |
| Escitalopram | Loxalate | Viatris Limited |
| Fluoxetine | **Arrow Fluoxetine (capsule)** | Teva Pharma (New Zealand) Limited |
| Fluoxetine | Arrow Fluoxetine (dispersible tablet) | Teva Pharma (New Zealand) Limited |
| Fluoxetine | Fluox capsule | Viatris Limited |
| Fluoxetine | **Fluox dispersible tablet** | Viatris Limited |
| Paroxetine | Aropax | GlaxoSmithKline NZ Limited |
| Paroxetine | **Loxamine** | Viatris Limited |
| Paroxetine | Paxtine | Viatris Limited |
| Sertraline | **Setrona** | Douglas Pharmaceuticals Limited |
| Venlafaxine | **Efexor XR** | Viatris Limited |
| Venlafaxine | Enlafax | Viatris Limited |

*Products with a published data sheet. Additional products are approved but not available.*

| | |
|---|---|
| PHARMAC funding | Products funded by PHARMAC are highlighted in **bold**. |
| Previous MARC meetings | September 2019: Serotonin reuptake inhibitor and persistent sexual dysfunction |
| International action | See section 4. |
| *Prescriber Update* | Sexual dysfunction associated with antidepressants and antipsychotics (*Prescriber Update 36(1): 5-7 March 2015*) |
| Other publications | Medsafe consumer medicine information leaflet: Medicines for depression or other mental disorders and difficulties with sex (sexual dysfunction) (March 2016). |
| Classification | Prescription medicine |
| Usage data | See section 2.1.2 |

| | |
|---|---|
| Advice sought | **The Committee is asked to advise:**<br>• Whether for sexual dysfunction with SSRIs/SNRIs (in general), is the current information in the data sheets sufficient to manage this risk? If no, what updates are needed?<br>• On the strength of the evidence for an association between SRIs and the syndrome post-SSRI sexual dysfunction (PSSD) whether the evidence warrants updates to the data sheets for SRIs.<br>• Whether any communication is required other than in MARC's remarks? |

# Table of Contents

# 1 PURPOSE

An Expert Working Group of the Commission on Human Medicines (CHM) in the UK recently concluded their review into how potential risks associated with antidepressant medicines are communicated to patients within the Patient Information Leaflets (PILs) [1].

This review was launched after concerns were raised by families and patients that current safety warnings in the PILs did not clearly explain certain side effects [1].

Recommendations to the Medicines and Healthcare Products Regulatory Agency (MHRA) following the review included that the wording of several PILs should be updated to better reflect patient feedback and emerging evidence on the potential for sexual dysfunction that may continue after stopping treatment [1].

A warning that long-lasting sexual dysfunction following discontinuing of treatment with selective serotonin reuptake inhibitors (SSRIs) and serotonin and noradrenaline reuptake inhibitors (SNRIs) have been reported, is currently listed in section 4.4 of the data sheets for these medicines [2].

The purpose of this report is to provide an update on this safety issue.

# 2 BACKGROUND

At the September 2019 Medicines Adverse Reaction Committee (MARC) meeting, Medsafe sought advice on serotonin reuptake inhibitors (SRIs) and persistent sexual dysfunction after discontinued treatment. The review by Medsafe followed a notification from RxISK (an independent drug safety website) of a recently published study that investigated clinical reports of sexual dysfunction, including post-SSRI sexual dysfunction (PSSD) [3, 4].

On review of the available information, the Committee recommended that updates to the data sheet were necessary [4].

The report and minutes from the September 2019 meeting are published on the Medsafe website.

**Comments**

This report will focus on new information available since previous time that this topic was presented to the MARC.

This update includes the following SRIs:

- SSRIs: Citalopram, escitalopram, fluoxetine, paroxetine and sertraline.
- SNRIs: Venlafaxine.

It is acknowledged that other antidepressants may cause sexual disruption.

This report will review SSRIs and SNRIs only.

## 2.1 Serotonin reuptake inhibitors (SRIs)

### 2.1.1 Indications

Table 1 outlines the indications of approved SRIs products with a published data sheet in New Zealand.

**Table 1: Indications of approved serotonin reuptake inhibitor medicines with a published data sheet in New Zealand**

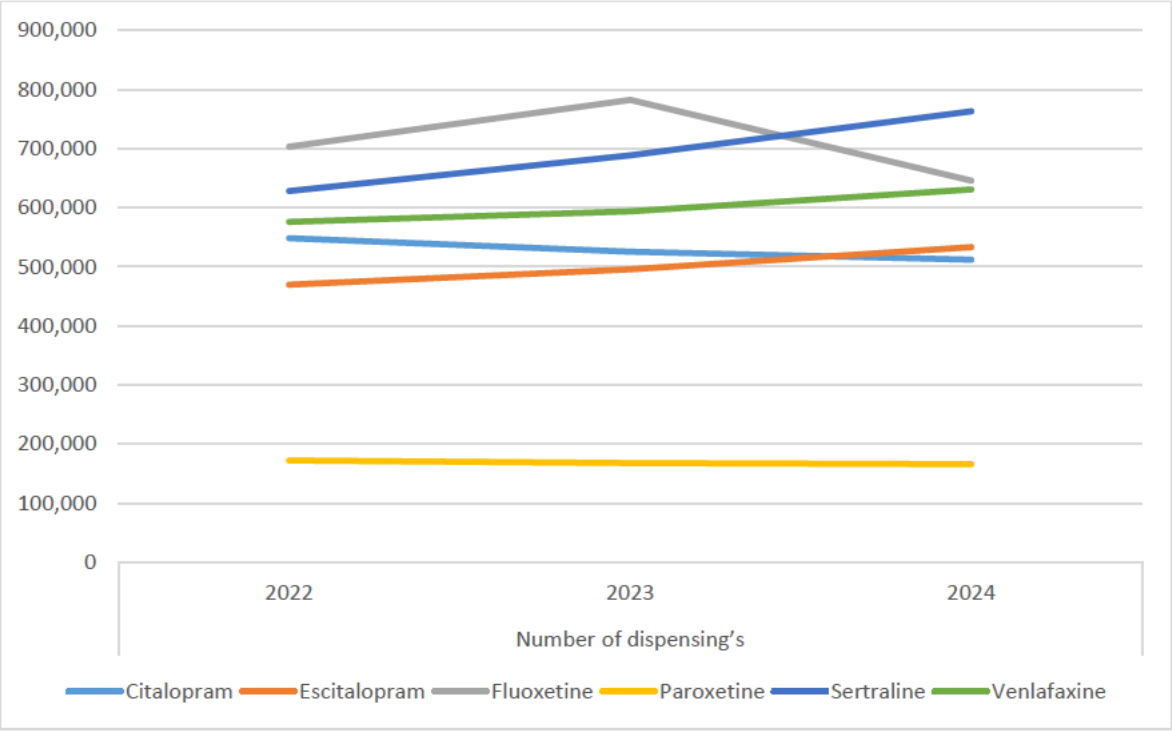
| SRI | Indication |
|---|---|
| *Selective serotonin reuptake inhibitor (SSRI)* | |
| **Citalopram** | |
| Celapram<br>Cipramil | Adults:<br>• Depressive illness in the initial phase and as maintenance against potential relapse/recurrence |
| **Escitalopram** | |
| Escitalopram-Apotex<br>IPCA-Escitalopram<br>Lexapro<br>Loxalate | Adults:<br>• Major depression<br>• Social anxiety disorder (social phobia)<br>• Generalised anxiety disorder<br>• Obsessive-compulsive disorder |
| **Fluoxetine** | |
| Arrow-Fluoxetine Capsule/tablet<br>Fluox capsule/tablet | Adults:<br>• Depression and its associated anxiety<br>• Bulimia nervosa<br>• Obsessive-Compulsive disorder<br>• Premenstrual dysphoric disorder (PMDD) - a severe form of PMS. |
| **Paroxetine** | |
| Aropax<br>Loxamine<br>Paxtine | Adults:<br>• Major depressive disorder<br>• Obsessive compulsive disorder<br>• Panic disorder<br>• Social anxiety disorder/social phobia<br>• Generalised anxiety disorder<br>• Post traumatic stress disorder |
| **Sertraline** | |
| Setrona | Paediatric patients (6 – 17 years of age):<br>• Obsessvie - compulsive disorder<br>Adults:<br>• Symptoms of depression, including depression accompanied by symptoms of anxiety, in patients with or without a history of mania<br>• Obsessive-compulsive disorder<br>• Panic disorder, with or without agoraphobia<br>• Post-traumatic stress disorder<br>• Social phobia (social anxiety disorder)<br>• Premenstrual dysphoric disorder |
| *Serotonin and noradrenaline reuptake inhibitor (SNRI)* - **Venlafaxine** | |
| Efexor-XR<br>Enlafax XR | Adults:<br>• Major depression<br>• Generalised anxiety disorder<br>• Social anxiety disorder<br>• Panic disorder<br>• Prevention of relapse and recurrence of major depression where appropriate. |

Source: Medsafe Product Application Search, accessed 26 March 2026.

### 2.1.2 Usage

Figure 1 outlines the number of dispensings from a community pharmacy from 2022 to 2024, using data from the Pharmaceutical Web Tool.

**Figure 1: Number of dispensings of SSRIs/SNRIs 2022 – 2024 (Pharmaceutical Web Tool)**




*Number of dispensings: Number of times the pharmaceutical product is dispensed from a pharmacy to the named person on all occasions including repeats (except for administrative dispensing's such as owed balances) during the year.*

*Source: Health New Zealand. 2025. Pharmaceutical Data web tool version 14 August 2025 (data extracted from the Pharmaceutical Collection on 4 June 2025). URL: https://tewhatuora.shinyapps.io/pharmaceutical-data-web-tool/ (Accessed 26 March 2026)*

Table 2 outlines the number of people who reiceved a dispensing for SSRIs/SNRIs from 2022 to 2024.

**Table 2: Number of people who received a dispensing for SSRIs/SNRIs 2022 – 2024 (Pharmaceutical Web Tool)**

| SSRI/SNRI | Number of people who received a dispensing | | |
|---|---|---|---|
| | 2022 | 2023 | 2024 |
| **Citalopram** | 95,556 | 90,185 | 84,999 |
| **Escitalopram** | 87,618 | 92,080 | 95,764 |
| **Fluoxetine** | 87,502 | 85,869 | 85,250 |
| **Paroxetine** | 27,236 | 26,210 | 25,279 |
| **Sertraline** | 114,526 | 126,283 | 136,932 |
| **Venlafaxine** | 58,192 | 59,022 | 60,632 |
| **Total:** | **470,630** | **479,649** | **488,856** |

*NumPpl: Number of people who received a dispensing of the pharmaceutical product as a named person from a pharmacy at least once during the year (includes people who only received a repeat dispensing during the year.*

*Source: Health New Zealand. 2025. Pharmaceutical Data web tool version 14 August 2025 (data extracted from the Pharmaceutical Collection on 4 June 2025). URL: https://tewhatuora.shinyapps.io/pharmaceutical-data-web-tool/ (Accessed 26 March 2026).*

**Comments**

It can be approximated around 10% of the NZ population were dispensed an SSRIs/SNRIs from a community pharmacy in 2024. The data above does not include SSRI/SNRI that are used in hospitals.

The number of people who have been dispensed SSRIs/SNRIs from a community pharmacy in NZ has increased between 2022 to 2024.

## 2.2 Sexual dysfunction

### 2.2.1 Overview

#### *2.2.1.1 Definition*

In general, 'sexual dysfunction' includes the following components:

- Impaired sexual function, such as disorders of sexual drive (usually loss of libido), disorders of arousal and disorders or orgasm and ejaculation [5,6].
- Clinically significant distress, sadness or worry regarding the impaired sexual function and its consequences [5].

A formal diagnosis includes sexual dysfunction that cannot be fully attributed to another medical or mental health condition and must be present for a minimum amount of time (typically 6 months) [5].

Sexual problems that do not meet the formal diagnostic criteria can also occur [5].

#### *2.2.1.2 Additional information*

Sexual dysfunction is common in both men and women [7].

Causes of sexual dysfunction include variations in hormone levels, medical illnesses, medicines, lifestyle factors or attitude towards sex/intimate partner [7,8].

Sexual dysfunctions are multifactorial and influenced by biological, psychological, interpersonal and sociocultural factors [5].

Between 50% and 70% of individuals with depression experience sexual dysfunction. Symptoms associated with sexual dysfunction that occur due to depression predominantly include low sex drive (both sexes), with disorders of arousal and orgasm or ejaculation occurring less commonly [6, 8].

Assessment of sexual dysfunction in an individual includes taking a detailed sexual history, psychological and physical assessment and use of questionnaires and symptom scales [5].

**Comments**

Sexual dysfunction is common in people with depression.

The ongoing burden of symptoms can have significant emotional and psychological impacts.

### 2.2.2 SRI induced sexual dysfunction

Sexual dysfunction is common side effect associated with SRI treatment [6].

Symptoms listed in SSRI and SNRI (venlafaxine) data sheets include ejaculation disorders, erectile dysfunction, libido decreased, priapism and anorgasmia [9].

Systematic review and meta-analyses have highlighted that SSRI treatment significantly increases the risk of sexual dysfunction, particularly orgasmic dysfunction and reduced sexual satisfaction [10].

It has been reported that with SSRIs/SNRIs, 27–65% of female patients and 26–57% of male patients experienced either a deterioration of pre-existing difficulties or the onset of new sexual problems during the initial weeks of treatment [9].

Sexual side effects of SRIs usually persist for as long as the medicine is taken and resolve after discontinuation. However, continued symptoms despite discontinuation have been reported and the syndrome 'post-SSRI sexual dysfunction (PSSD)' has been used to describe these side effects [8].

*2.2.2.1 Potential mechanisms*

Sexual function involves complex interactions between multiple neurotransmitters including serotonin (5-HT), noradrenaline, dopamine and acetylcholine [10].

5-HT appears to be the main neurotransmitter that can impact sexual function [6].

Increased synaptic cleft serotonin concentrations caused by serotonin reuptake inhibition, leads to enhanced activation of post-synaptic 5-HT receptors (particularly 5-HT2A and 5-HT3), which has an inhibitory sexual effect [9].

It is proposed that effects on orgasmic function are likely due to 5-HT inhibitory effects on spinal ejaculatory reflexes and the neural circuits controlling orgasm [9].

Negative effects on sexual desire and arousal are thought to be due to increased 5-HT activity that suppresses dopaminergic neurotransmission in key regions of the brain such as the nucleus accumbens and hypothalamus, areas important for these functions [9].

*2.2.2.2 Clinical implications and patient experiences*

Sexual dysfunction with SRIs is a common reason for treatment non-adherence and discontinuation [9].

The reporting of sexual dysfunction with SRIs is likely underestimated. Symptoms may be attributed to other causes, rather than the medicine itself. Reporting sexual side effects can be challenging as it may be considered shameful or embarrassing [9].

Experiencing sexual related side effects significantly impacts an individual's self-esteem, quality of life, mood and partner relationships [9].

Routine review of sexual function by healthcare professionals before and during treatment can provide important information about either decline or improvement in sexual function [6, 9].

Strategies suggested for managing antidepressant-induced sexual dysfunction include watch and wait, reduce dose, change administration times and drug holidays [6].

**Comments**

Sexual dysfunction is a common concern among both males and females and may be caused by multiple factors, including medicines.

While depression itself is often associated with sexual dysfunction, the use of an antidepressant may exacerbate this by causing more sexual dysfunction. This presents a complex clinical challenge in individuals who experience symptoms.

Due to the nature of the side effect, the prevalence of the condition is not clear. However, SRI-induced sexual dysfunction appears commonly experienced by individuals taking these medicines. A range of sexual related side effects have been reported and sexual related ADRs are listed in the data sheets.

Continued symptoms despite discontinuation have also been reported and such reports led to updates to prescribing information for SRIs internationally.

Sexual related symptoms caused by SRIs have the potential to be severe and negatively impact an individual's quality of life. It is important that patients are informed about the possible side effects and healthcare professionals should enquire about symptoms before and during treatment

Additional literature articles have been published about persisting sexual dysfunction after treatment discontinuation with SRIs since the topic was discussed at the September 2019 MARC-meeting, including referring to the syndrome PSSD.

PSSD advocacy groups campaign for broader public awareness for PSSD around the world.

## 2.3 Data sheets

### 2.3.1 New Zealand

#### *2.3.1.1 Section 4.4*

All the published SRI data sheets (except for fluoxetine) include a warning regarding sexual dysfunction including long-lasting sexual dysfunction after treatment discontinuation. This information is reflected in the consumer medicine information leaflet (CMI).

**Table 3: Information on persistent sexual dysfunction in SSRI and SNRI data sheets and CMIs**

| | |
|---|---|
| **Data sheet** | **Section 4.4**<br>*Sexual dysfunction*<br>Selective serotonin reuptake inhibitors (SSRIs)/serotonin norepinephrine reuptake inhibitors (SNRIs) may cause symptoms of sexual dysfunction (see section 4.8). There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRI. |
| **CMI** | Tell your doctor or pharmacist if you notice any of the following and they worry you:<br>• sexual function problems: such as delayed ejaculation, problems with erection, decreased sex drive or difficulties achieving orgasm (In some cases, these symptoms have continued after stopping treatment) |

Source: Viatris Limited. 2025. *Celapram New Zealand Data Sheet* 26 November 2025. URL: www.medsafe.govt.nz/profs/Datasheet/c/celapramtab.pdf (accessed 5 May 2026). Viatris Limited. 2025. Celapram New Zealand Consumer Medicines Information. URL: www.medsafe.govt.nz/consumers/CMI/c/celapram.pdf (accessed 5 May 2026).

**Comments**

Updates to SSRI and venlafaxine data sheets to include a warning on sexual dysfunction, including reports of long-lasting sexual dysfunction after discontinuation of treatment, occurred following the advice provided by the MARC at the September 2019 meeting.

The updated data sheets currently have the same warning noted to be recommended by EMA PRAC following their review on this safety issue in 2019.

**Summary of product characteristics**

4.4. Special warnings and precautions for use

Sexual dysfunction

Selective serotonin reuptake inhibitors (SSRIs)/serotonin norepinephrine reuptake inhibitors (SNRIs) may cause symptoms of sexual dysfunction (see section 4.8). There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRI.

**Package leaflet**

2. What you need to know before you take [Invented name]

Warnings and precautions

Medicines like [Invented name] (so called SSRIs/SNRIs) may cause symptoms of sexual dysfunction (see section 4). In some cases, these symptoms have continued after stopping treatment.

PSSD, the syndrome used in the literature to describe long-lasting sexual dysfunction after treatment discontinuation, is not referred to in the data sheet warning.

The current warning in the data sheet refers to the risk of sexual dysfunction with SSRIs/venlafaxine on treatment. For reports where symptoms continued after discontinuation this is referred to as 'long-lasting' sexual dysfunction.

The current warning does not appear to provide any additional information about what sexual side effects may occur on treatment, noting that many sexual related adverse effects are reported as common in section 4.8.

The information provided does not include any advice to healthcare professionals, such as monitoring that may be required or management options.

Data sheets for fluoxetine containing medicines (FLUOX capsule, FLUOX tablet, Arrow Fluoxetine capsule, Arrow Fluoxetine dispersible tablet) do not include the above warning. However, sexual dysfunction (occasionally persisting after treatment discontinuation) is listed in section 4.8 (see below).

#### *2.3.1.2 Section 4.8*

Table 4 below shows the listed sexual side effects listed in section 4.8 of the SSRI and SNRI data sheets.

**Table 4: Sexual side effects listed in section 4.8 of SSRI and SNRI data sheets**

| Product name | Section 4.8 | |
|---|---|---|
| ***Citalopram*** | | |
| Celepram | Clinical trials:<br>• ejaculation disorders 5.9% (*statistically significant versus placebo)<br>• impotence (2.8%)<br>• libido decreased (2.5%) | Other side effects:<br>• increased libido (unknown)<br>• priapism (unknown) |
| | Male and female sexual dysfunction with SSRIs<br>While sexual dysfunction is often part of depression and other psychiatric disorders, there is increasing evidence that treatment with selective serotonin reuptake inhibitors (SSRIs) may induce sexual side effects. This is a difficult area to study because patients may not spontaneously report symptoms of this nature, and therefore, it is thought that sexual side effects with the SSRIs may be underestimated. In placebo-controlled clinical trials (table), the reported incidence of decreased libido for the whole population was 2.5%; ejaculation disorder (primarily ejaculatory delay), and impotence in male depressed patients receiving citalopram (N=423) was 5.9%, and 2.8%, respectively. In female depressed patients receiving citalopram (N=660), the reported incidence of anorgasmia was 0.5%. The reported incidence of decreased libido was 0.4% among depressed patients receiving placebo, whilst sex specific adverse events were not reported among male and female depressed patients receiving placebo.<br><br>While it is difficult to know the precise risk of sexual dysfunction associated with the use of SSRIs, physicians should routinely inquire about such possible side effects. | |
| ***Escitalopram*** | | |
| ICPA-escitalopram | Clinical trials:<br>• libido decreased (3.9%*)<br>• impotence (2.2%*)<br>• anorgasmia female (2.9%)*<br>• ejaculation disorder (4.7%*)<br>• ejaculation failure (2.7%*)<br><br>*Statistically significant versus placebo | Other side effects:<br>• loss of libido (unknown),<br>• reproductive disorders/female: sexual function abnormality (unknown)<br>• reproductive disorders/male: ejaculation delayed (unknown), priapism. |
| ***Fluoxetine*** | | |
| Fluox | Clinical trials:<br>• abnormal ejaculation (common)<br>• impotence (common)<br>• anorgasmia (uncommon)<br>• sexual dysfunction (occasionally persisting after treatment discontinuation) (uncommon)<br>• priapism (rare) | Post market:<br>• enlarged clitoris (unknown) |
| ***Paroxetine*** | | |
| Aropax | Clinical trials/post market:<br>• sexual dysfunction (very common)<br>• priapism (rare) | |

| | | |
|---|---|---|
| ***Sertraline*** | | |
| Setrona | Clinical trials:<br>• ejaculation disorder (common)<br>• sexual dysfunction (common) | Post market:<br>• libido decreased (common)<br>• premature ejaculation (rare)<br>• priapism (rare) |
| ***Venlafaxine*** | | |
| Efexor XR | Clinical trials/post market:<br>• libido decreased (common)<br>• anorgasmia (common)<br>• abnormal organism (uncommon)<br>• erectile dysfunction (common)<br>• ejaculation disorder (common). | |

Source: Medsafe Product Application Search, accessed 26 March 2026.

**Comments**

There are slightly different side effects noted between the data sheets. Not all data sheets include decreased/loss of libido. Some data sheets list 'sexual dysfunction' with several or with few other sexual related symptoms additionally listed.

When 'sexual dysfunction' is listed as a side effect, it is used in a broad sense. It would be helpful if specific symptoms were also listed.

### 2.3.2 International prescribing information

#### *2.3.2.1 Information on sexual dysfunction post discontinuation*

The prescribing information in Australia and UK includes the same warning for sexual dysfunction that is in the data sheets [11, 12].

The following information is included in the Prozac (fluoxetine) label in the US relating to a warning for sexual dysfunction [13].

**5.17 Sexual Dysfunction**

Use of SSRIs, including PROZAC, may cause symptoms of sexual dysfunction [see Adverse Reactions (6.1)]. In male patients, SSRI use may result in ejaculatory delay or failure, decreased libido, and erectile dysfunction. In female patients, SSRI use may result in decreased libido and delayed or absent orgasm.

It is important for prescribers to inquire about sexual function prior to initiation of PROZAC and to inquire specifically about changes in sexual function during treatment, because sexual function may not be spontaneously reported. When evaluating changes in sexual function, obtaining a detailed history (including timing of symptom onset) is important because sexual symptoms may have other causes, including the underlying psychiatric disorder. Discuss potential management strategies to support patients in making informed decisions about treatment.

'Symptoms of sexual dysfunction occasionally persist after discontinuation of fluoxetine' is included in the adverse reaction section. Similar wording for this ADR does not appear to be included in the citalopram, sertraline or venlafaxine product labels [14].

The following information is included in an escitalopram product monograph from Canada [15]:

**7. Warnings and precautions**

Reproductive health: Female and male potential

Function: Selective serotonin reuptake inhibitors (SSRIs) may cause symptoms of sexual dysfunction. Patients should be informed that there have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs.

**9. Adverse reactions**

Male and Female Sexual Dysfunction with SSRIs

While sexual dysfunction is often part of depression and other psychiatric disorders, there is increasing evidence that treatment with selective serotonin reuptake inhibitors (SSRIs) may induce sexual side effects. Furthermore, there have been reports of long-lasting sexual dysfunction where these symptoms have continued despite discontinuation of SSRIs. This is a difficult area to study because patients may not spontaneously report symptoms of this nature, and therefore, it is thought that sexual side effects with SSRIs may be underestimated.

**Comments**

The FDA label for Prozac includes additional information in the warning for sexual dysfunction compared to warnings in SSRI/venlafaxine data sheets. This information is seen as important information for healthcare professionals.

Canadian product monograph for escitalopram contains additional information in relation to the reports of long-lasting sexual dysfunction discontinuation, including how this area is difficult to study and that sexual side effects with SSRIs may be underestimated.

Healthcare professionals are recommended to advise patients that there have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs.

# 3 SCIENTIFIC INFORMATION

The literature was reviewed for any recent available information for PSSD (2019 to 2026) noting that the previous MARC paper reviewed earlier literature on this topic.

## Search Strategy

**Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily <1946 to May 13, 2026> (adapted for PsycInfo, Scopus, and Embase)**
**Search Strategy:**

1 Selective Serotonin Reuptake Inhibitors/
2 ("Selective Serotonin Reuptake Inhibitor*" or SSRI*).tw.
3 "Serotonin and Noradrenaline Reuptake Inhibitors"/
4 ("Serotonin and Noradrenaline Reuptake Inhibitor*" or SNRI*).tw.
5 "antidepress*".m_titl.
6 1 or 2 or 3 or 4 or 5
7 ((post* or peristent) adj2 (sexual or genital or arousal)).mp.
8 (PSSD or "post-ssri sexual dysfunction").mp.
9 7 or 8
10 6 and 9
11 8 or 10
12 limit 11 to (english language and yr="2018 -Current")

## 3.1 Systematic reviews

### 3.1.1 Selective serotonin reuptake inhibitors, post-treatment sexual dysfunction and persistent genital arousal disorder (Tarchi et al, 2023) [15]

The aim of this systematic review was to identify existing evidence of sexual dysfunction following SSRI discontinuation (PSSD) and to provide information on reported symptoms and proposed treatment options. In addition, the authors sought to establish whether current literature allows estimates of prevalence.

Observational studies, case reports and case series with clinical data regarding SSRI use and sexual dysfunction, either persisting or presenting after treatment discontinuation, were were included. The search included articles published in English up to December 2022.

A total of 19 studies were selected (including retrospective interventional studies, observational studies and case reports).

Information on adverse effects from the review relating to onset, symptoms and differential diagnosis is summarised in the table 5 below.

**Table 5: Summary of reported PSSD (adapted from Tarchi et al, 2023)**

| Onset | Reported symptoms | Differential diagnosis |
|---|---|---|
| Most studies showed evidence of sexual dysfunction during SSRI treatment that continued after discontinuation | Symptoms varied and differed between sexes.<br>Symptoms:<br>• Sexual: penile anaesthesia, pleasureless orgasm, loss of libido, difficulty achieving orgasm, loss of nocturnal erections, reduced seminal volume, testicular pain, reduced penis size, premature ejaculation, watery ejaculate, slow leakage of ejaculate, and<br>• Non-sexual: emotional blunting, reduced sense of taste and smell.<br>Most reported symptoms overlap with side effects described during SSRI treatment or with general symptoms of depression except for nipple and genital anaesthesia. | Depressive and anxiety disorders can cause sexual dysfunction, and these symptoms may overlap with SSRIs.<br>SSRIs interruption could expose an underlying residual depressive symptomatology or worsening of the clinical condition. |

The prevalence of PSSD was not able to be estimated from available studies due to the study designs.

A summary of the case reports presented in the review is shown in table 6 below.

**Table 6: Summary of PSSD case reports (adapted form Tarchi et al, 2023)**

| References | Case(s) description | Symptoms | Onset |
|---|---|---|---|
| Bolton 2006 | 26, M, sertraline | Genital anaesthesia, decreased libido, delayed orgasm, anorgasmia, decreased genital tactile sensation | Initiation of treatment and persisted thereafter. |
| Calabro 2019 | 23, M, citalopram | Loss of libido, erectile dysfunction, anejaculation | Immediately after administration and continued 3 months post stopping. |
| Csoka 2006 | 20's, F, fluoxetine | Reduced libido, decreased genital and nipple tactile sensation, anorgasmia | Onset initiation of treatment, persisted long after discontinuation |
| Csoka 2006 | 20's, F, citalopram | Anorgasmia, ED, reduced libido, decreased genital tactile sensation | Onset initiation of treatment, persisted long after discontinuation |
| Csoka 2006 | 20's, F, sertraline | Loss of libido, partial anorgasmia, reduced ejaculate volume, and genital numbness | Onset initiation of treatment, persisted long after discontinuation |
| Csoka 2008 | M, fluoxetine | Pleasureless orgasm, genital anaesthesia, difficulty maintaining and achieving erection | During treatment and persistent thereafter |
| Csoka 2008 | M, citalopram | Pleasureless orgasm, genital anaesthesia, difficulty maintaining and achieving erection | During treatment and persistent thereafter |
| Csoka 2008 | M, paroxetine, sertraline, venlafaxine | Weak erection, continuous, slow leakage of seminal fluid during sexual activity but prior to ejaculation, significantly decreased genital sensitivity, and anorgasmia | During treatment and persistent thereafter |
| Korda 2009 | F, paroxetine | Anorgasmia, unwanted genital arousal, Genital pulsing, tingling, engorgement, pressure, swelling, lubrication not related to sexual desire, excitement, thoughts, or fantasies. Vaginal pain either throbbing, sharp or burning | After abrupt discontinuation of paroxetine (duration not reported) |
| Patacchini 2020 | 21, M, sertraline | Premature ejaculation, physical impotence, absence of libido and sexual pleasure, tactile, and temperature anaesthesia in the genital area, emotional flattening. | After gradual discontinuation of sertraline (duration not reported) |

The authors conclude that the current evidence on individuals who experience PSSD is limited by uncertain inclusion criteria in the sampling process, selection bias in recruiting participants (online surveys) and inadequate controlling for potentially confounding factors.

The authors consider a high quality observational longitudinal study with sufficient statistical power and supported by clinical diagnostic interviews is needed before definitive accounts of the condition can be provided.

**Comments**

While the authors note there were limitations, case reports of persistent sexual dysfunction included both those that started during treatment (including at initiation) and continued after discontinuation and symptoms occurring post discontinuation only.

The authors note that determine the cause of the PSSD is difficult as it could also be due to an underlying residual depressive symptomatology or a worsening of the condition.

The authors consider that, nipple and genital anaesthesia have been reported in association with PSSD but are not fully explained by depressive or anxious symptoms and may possibly point towards a pharmacological cause.

## 3.2 Observational/retrospective studies

### 3.2.1 Frequency of self-reported persistent post-treatment genital hypoesthesia among past antidepressant users: a cross-sectional survey of sexual and gender minority youth in Canada and the US (Pirani et al, 2025) [16]

This study aimed to estimate the frequency of persistent post-treatment genital hypoesthesia (PPTGH) among UnACoRN participants who self-reported past use and discontinuation of antidepressant medicines compared to other psychiatric medicines.

UnACoRN was a voluntary online cross-sectional youth survey (15 – 29 years of age) of 7,037 residents from Canada and 2,532 residents from the US. Participants were asked approximately 135 non-randomised questions.

Participants who had reported surgeries to the genital area and those without sexual experience were excluded.

As part of the survey, participants were asked questions about psychiatric medicine use and sexual dysfunction symptoms. Those who reported previous or current use of psychiatric medicine were asked about a list of PSSD related symptoms. Participants reporting any PSSD-related symptoms were asked whether they were currently taking the medicine. Participants who had discontinued the medicine were asked if the symptoms continued after stopping the medicine.

Criteria used to diagnose PSSD was prior treatment with SRI and an enduring change in genital sensation upon treatment cessation. While participants could provide information about any PSSD related symptoms, analysis focused on genital hypoesthesia only (PPTGH).

The association between medicine class use and the presence of both genital hypoesthesia and symptom persistence was analysed by using logistic regression. Adjusted analysis was also undertaken for age, sex at birth and gender-affirming hormonal treatment. Further adjusted analysis included depression severity.

*Results*

Among all the UnACoRN respondents, 2,179 were included in the analysis. The median age of participants was 20 years old. Most (88.8%) participants were assigned female at birth, identified as white (80.%) and resided in Canada (77.8%).

A total of 574/2179 respondents reported genital hypoesthesia with psychiatric medicines. These respondents were older, more likely to report assigned male at birth and to have used all types of psychiatric medicines.

Among those who had taken antidepressants (alone or in combination with other psychiatric medicines), 218/707 reported genital hypoesthesia, of which 93 reported persistent symptoms after discontinuation (Table 7).

Among 98 participants who took sedatives and/or antipsychotics but not antidepressants, 8 reported genital hypoesthesia, of which 1 reported persistent symptoms (Table 7).

**Table 7: Frequency and proportion of genital hypoesthesia and genital hypoesthesia plus symptoms persistence among those who had stopped psychiatric treatment**

For participants who had stopped treatment, bivariate analyses showed past use of antidepressants (p=0.001) and antipsychotics (p=0.002) were independently associated with persistent post-treatment genital hypoesthesia. However, after controlling for concomitant treatments, only past antidepressant users had consistently increased odds of reported persistent post-treatment genital hypoesthesia.

The adjusted analyses showed past antidepressant users had 14.2 times higher odds of persistent post-treatment genital hypoesthesia compared to those who had not taken antidepressants (adjusted OR 14.2 (95% CI 2.92, 257).

Past use of sedatives (adjusted OR 1.73, 95% CI 1.03, 2.89) and severe depression (OR 3.66, 95% CI 1.18,16.1) was also associated with increased odds of reporting persistent post-treatment genital hypoesthesia.

The authors concluded that these findings support concerns that for some antidepressants, long-lasting sexual side effects after discontinuation can occur and clearer warnings are needed. In addition, further research is needed into PSSD.

**Comments**

An advantage to this study was that the survey was not specifically aimed at people who had side effects from medicines, including PSSD.

The study had several limitations including self-reporting of symptoms, that the population sample may not generalise to all populations and that only the symptom of genital hypoesthesia was used to diagnose PSSD.

Due to the nature of the study design, a direct comparison of people who had used antidepressants only with those who had not used antidepressants was not possible. While a higher number of PPGTH was identified in past antidepressant users, the presence of other psychiatric medicines is a confounding factor.

This study was also not able to distinguish if genital hypoesthesia was due to other non-medicine causes.

Another limitation was that the comparison group of 'other psychiatric medicines' was relatively small compared to 'antidepressant users' (102 versus 707), and 1 participant reported PPGTH. This very small number of events contributed to the striking adjusted OR (around 14) and the large CI. Therefore, the OR should be interpreted cautiously.

### 3.2.2 Sexual symptoms and biological pathophysiology of post-SSRI sexual dysfunction: A 15-year review (Goldshien et al, 2025) [17]

*[Abstract only]*

This study was a retrospective chart review of men diagnosed with PSSD to assess frequency and severity of sexual symptoms and biologic pathophysiology.

Men with various sexual dysfunctions who met inclusion criteria for PSSD between 2009 and 2024 were reviewed.

Patients with a history of erectile dysfunction (ED) following blunt penile/perineal trauma, 5-alpha reductase inhibitor use or exposure to ≥2 vascular risk factors were excluded.

A total of 43 men, mean age 27.6 years (range 16 – 43) were included in the analysis.

Patients reported multiple sexual health concerns included ED (88%), reduced genital sensation (92%), low libido and orgasmic dysfunction. Significant psychological distress related to symptoms was also reported.

Patients also underwent physical testing. Hormonal testing including testosterone, dihydrotestosterone, estradiol, prolactin, LH, FSH and sex hormone binding globulin values in this cohort were not consistent with hormonal pathophysiology for symptoms.

The mean International Index of Erectile Function (IIEF) of patients presented with ED from PSSD was 8.8 +/- 8, consistent with severe ED. Grayscale ultrasound findings revealed erectile tissue inhomogeneity.

Quantitative sensory testing including vibration, heat and cold perception threshold test revealed 89% of patients had abnormal results.

The authors conclude that in the population studied, PSSD occurring in young, healthy men is associated with severe ED and multiple other persistent sexual dysfunctions.

**Comments**

Despite being young and healthy, very high rates of persistent symptoms of ED and reduced genital sensation were reported.

In addition to self-reported symptoms, physiological testing took place. Penile tissue ultrasound abnormalities were identified that resembled patterns seen in older men with vascular erectile dysfunction.

The authors interpret this a possible smooth muscle damage within the erectile tissue due to SSRI/SNRI induced oxidative stress and cell death causing long-term structural changes. It is proposed that this mechanism could explain persistent ED after medicine discontinuation.

### 3.2.3 Estimating the risk of irreversible post-SSRI sexual dysfunction (PSSD) due to serotonergic antidepressants (Ben-Sheetrit et al, 2023) [18]

This was a retrospective cohort analysis that investigated the risk of ED and PSSD in males treated with serotonergic medicines over a 19-year period using a healthcare database in Israel.

The aims of the study were to:

(1) To assess the risk of ED* in males with and without a history of serotonergic antidepressants, in the absence of medical or psychiatric comorbidities or other medicines associated with ED.
(2) To estimate the prevalence of PSSD** in males as evidenced by treatment-emergent ED treated with PDE-5 inhibitors persisting after discontinuation of antidepressant treatment and no active diagnosis of depression or anxiety.

*ED was defined as one or more prescription of PDE-5 inhibitor during the study period.

**PSSD was defined as treatment-emergent sexual dysfunction (ED) following the use of one or more serotonergic antidepressants that persists despite the cessation of antidepressant treatment for one month or more.

Table 8 below outlines the inclusion and exclusion criteria for the study.

**Table 8: Inclusion and exclusion criteria (Ben-Sheetrit et al, 2023)**

| | |
|---|---|
| Inclusion criteria | male, aged between 20 and 50 years old, documented last BMI <25 |
| Exclusion criteria | medical or psychiatric comorbidities associated with ED, treatment with medicines known to cause ED, past or present use of 5a-reductase inhibitors, history of alcohol or substance use disorders, current or past smoking |

Statistical analysis

Chi-square tests for independence were used to compare the study and control groups on their use of PDE-5 inhibitors. A logistic regression model was fitted to assess association between history of serotonergic antidepressants use during the study period and the risk of developing erectile dysfunction.

Results

A total of 12,302 males were included in the study, of which 866 (7%) used serotonergic antidepressants during the study period (study group), compared to 11,436 who had not (control group).

Demographic information on study participants is outlined below in Table 9.

**Table 9: Demographic information (Ben-Sheetrit et al, 2023)**

Most participants used one antidepressant during the study period, with SSRIs being the most frequently used.

A total of 360 participants (2.9%) had used a PDE-5 inhibitor during the study period; 74 (8.5%) in the study group and 286 (2.5%) in the control group. This difference was statistically significant.

Serotonergic antidepressant use was significantly associated with PDE-5 inhibitor use (OR 3.6 [95% CI 2.8, 4.8], p<0.001) and this association remained significant when adjusted for age, SES, BMI, depression and anxiety [OR 3.2 [95% CI 2.3, 4.4], p<0.001].

Age was also found to be significantly associated with PDE-5 inhibitor use (OR 1.08 [95% CI 1.06, 1.1], p<0.001).

There were 4 participants who met the criteria for PSSD. They were aged 32, 34, 37 and 43 years old. They used antidepressants with at least a partial serotonergic mechanism for 4 – 8 months before initiating treatment with PDE-5 inhibitors. They continued to have erectile dysfunction after discontinuation of treatment evidenced by 3,6 – 14.8 months of PDE-5 inhibitor treatment at the end of the study period.

The prevalence of PSSD of males of ages 21 – 49 years of the population of database was calculated to be 4.3 per 100,000.

Discussion

The authors of this study found that after exclusion of confounding factors, treatment with serotonergic antidepressants was associated with more than a threefold increase in the risk of receiving PDE-5 inhibitor treatment for ED compared to controls and that PSSD developed in 0.46% (1 in every 216).

The authors conclude that the findings of this study indicate that treatment with serotonergic antidepressants is associated with a small but significant risk of irreversible sexual dysfunction after treatment discontinuation.

**Comments**

Results of this study found that antidepressant exposure was associated with higher risk of ED in the study population.

This study attempted to investigate the prevalence of PSSD in the study population, which from the results appears to be rare but possible.

This figure may underestimate the true prevalence for many reasons. Firstly, this study only included males, while females can experience PSSD also. Secondly, individuals may experience other symptoms that are consistent with PSSD and may therefore not have been captured in this study design.

While the exclusion criteria excluded other possible causes of sexual dysfunction, it is not known whether the prescription for PDE-5 inhibitor was due to the side effects of the serotonergic medicine or for another cause.

### 3.2.4 Exposure to serotonin selective reuptake inhibitors or serotonin noradrenaline reuptake inhibitors and sexual dysfunction: results from an online survey (Patacchini et al, 2021) [19]

This was an online voluntary survey in individuals self-declaring to be affected by PSSD.

Inclusion criteria were: at least 18 years of age, at least one SSRI/SNRI treatment, occurrence of sexual dysfunction during SSRI/SNRI treatment or at discontinuation, self-reporting to be affected by PSSD.

Exclusion criteria were presence of self-declared sexual dysfunction before SSRI/SNRI treatment, self-declared diagnosis of organic damage/disease which might imply sexual dysfunction prior to or during the SSRI/SNRI treatment.

Subjects were invited through posts published in web forums to complete an online survey.

A total of 135 responses to the survey were analysed. Among these, 115 (85.2%) were males and 20 (14.8%) females. The mean age was 31.9 years (SD = 8.9, range 19–59 years).

On average participants had taken an SSRI/SNRI for a period of 117.7 ± 233.2 weeks (n = 134) and the time elapsed from the first dose and the occurrence of sexual dysfunction was 18.9 ± 53.4 weeks (n = 131).

There were 118 respondents (87.4%) that had sexual dysfunction while taking SSRI/SNRI, the rest had sexual dysfunction only at discontinuation.

Among all respondents in the survey, the most reported symptoms were decreased libido (89.6%), less pleasant or weak orgasm (74.1%) and genital anaesthesia (67.4%).

Non-sexual related side effects were reported infrequently and included lack of emotions (6.7%), body numbness (1.5%), brain fog (1.5%), sleep problems (1.5%) and anxiety (1.5%).

The most reported symptoms specific for males (n=115) were erectile dysfunction (81.7%), reduced seminal volume (52.2%), decreased penis size (37.4%) and premature ejaculation (31.3%).

The most reported symptoms specific for females (n=20) were vaginal lubrication problems (40%) and irregular menstruation (5%).

A total of 90 respondents reported a diagnosis of mental disorder prior to the onset of sexual dysfunction, with the most common diagnosis being depressive disorders (41.5%), anxiety disorders (38.5%), sleep disorders (15.6%) and obsessive compulsive disorder (14.1%).

Based on the results of the survey, the authors state that respondents self-declaring to be affected by PSSD present a specific syndrome which is more represented in young, single, Caucasian/white males after exposure to SSRI/SNRI at relatively high doses and for relatively long periods. In addition, sexual symptoms are on average severe and long-lasting.

The authors comment that this is the first study on PSSD suggesting that this is not a syndrome but an iatrogenic disorder.

**Comments**

A large proportion of the respondents were male. It is not known if PSSD is more prevalent in males, or more likely to be reported by them.

No information was collected on whether participants were experiencing depression or underlying mental health conditions when they stopped SSRI/SNRI. It is unclear from the information available whether respondents had medically confirmed PSSD and/or if other possible causes for sexual dysfunction were present.

### 3.2.5 Characterising post-SSRI sexual dysfunction and its impact on quality of life through an international online survey (Studt et al, 2021) [20]

This retrospective study was an online survey designed to better characterise the symptoms of PSSD, disease course, potential treatment and overall impact of this condition on quality of life.

Eligible individuals to complete the survey had to be between 18 and 99 years of age and had to report use of an SSRI, SNRI or antidepressant which either inhibit serotonin reuptake or modulate serotonin regulation.

Table 10 outlines the demographics of survey respondents.

**Table 10: Demographics of survey respondents (Studt et al, 2021)**

A total of 239 respondents were included in the analysis. Respondents came from 39 countries, including regions with known PSSD support groups including the US (36%), Germany (12%) and the UK (10%).

Most of the respondents were male. The median age of male and female respondents was 29 and 30 years of age. SSRIs were taken by 92% of the respondents, of which 40% were taking sertraline. Respondents had taken SRIs for different durations, including 22% for over 5 years and 5% for less than 7 days.

As part of the survey, respondents were asked about different sexual side effects they experienced while taking an SRI. More than 50% of the respondents reported decreased sex drive, difficulty becoming aroused, decreased genital sensation, muted or pleasureless orgasms, no arousal by visual stimuli or absence of sexual attraction while taking an SRI.

ED and delayed ejaculation were reported by 65% and 51% of male respondents, respectively. Vaginal dryness was reported by 47% of female respondents.

Respondents were also asked to report which sexual side effects either persisted or developed after discontinuation of treatment with an SRI (Table 11). The most common sexual side effects experienced while taking a serotonin reuptake inhibitor were also the most common e experienced after discontinuation.

Common symptoms experienced by more than 50% of respondents while on an SSRI were reported to persist or newly develop in up to 18% of respondents after the discontinuation of treatment. Soft glans, which was experienced by only 26% of male respondents during treatment was reported to persist or develop in 13% of respondents after discontinuation of treatment. Vaginal dryness was the only sexual side effect with complete resolution after the discontinuation of treatment with a serotonin reuptake inhibitor (Table 11).

**Table 11: Symptoms of sexual dysfunction experienced by respondents during and after treatment with a serotonin reuptake inhibitor (Studt et al, 2021)**

A total of 12% of respondents had received counselling regarding potential sexual side effects while taking a SRI. From those who did not receive counselling, 90% said that knowledge of potential sexual side effects would have prompted them to decline treatment and request different medicines or counselling options.

For symptoms post discontinuation of treatment, 15% of respondents experienced a decrease in the severity of symptoms of sexual dysfunction. Symptom severity was unchanged for 32% of respondents and 54% reported new or worsening symptoms. Overtime, these persistent symptoms improved in 45% of respondents, remained constant for 13% and worsened for 24%.

A total of 59% reported PSSD had an extremely negative effect on their quality of life, and 23% reported very negative effect.

The survey also asked respondents about what treatments they had sought and/or been offered for PSSD. These included different medicines, vitamins, supplements and counselling without clear success.

**Comments**

While this survey provided informative survey results of individuals with PSSD, the study has limitations. These include small sample size and that the study population of individuals with PSSD limit the ability to generalise results to others who are currently taking SRIs.

In addition, the information provided by the respondents who chose to complete the survey may be influenced by their personal experiences with PSSD, which may bias the results.

### 3.2.6 Post-SSRI sexual dysfunction (PSSD): Ten-year retrospective chart review (Waraich et al, 2020) [21]

*[Abstract only]*

This was a retrospective review performed of charts of male patients with PSSD from 2009 – 2019 at a sexual clinic in the US.

Patients reported their symptoms, completed sexual function questionnaires (International Index of erectile function, IEF-EF), penile doppler ultrasound and quantitative sensory testing for genital sensation.

A total of 43 male patients were included in the study (mean age 31 years (range 18 – 59 years of age)).

The most common symptom was erectile dysfunction (93%). The mean IIEF-EF score was 12.9/30 (low scores may indicate severe ED). Most participants reported the ED symptoms as severe (49%), followed by mild-moderate (24%).

For ED patients who underwent Doppler ultrasound, 23/29 had varying degrees of erectile tissue inhomogeneity. This might indicate vascular or structural abnormalities related to erectile tissue.

Concomitant sexual health concerns of HSDD (hypoactive sexual desire disorder), orgasmic dysfunction and decreased genital sensation were noted in 86% (38.43), 72% (31/43) and 67% (29/43) of patients.

For patients with orgasmic dysfunction and/or decreased genital sensation who underwent testing, 89% (25/28) had abnormal results.

The authors comment that the results of this study are consistent with other reports of PSSD. The participants were young, had ED (mostly severe) in most cases and frequently had HSDD, poor orgasm and decreased genital sensation.

**Comments**

While this study was in a small population compared to other studies, clinical assessment of ED and genital sensation in those reporting the symptoms took place. Abnormal results were identified in the majority of those that reported these symptoms.

The study population was taken from a sexual medicine clinic. These individuals may have more severe presentations and therefore may not be representative of most SSRI users.

## 3.3 Other information

### 3.3.1 Persistent sexual dysfunction after SSRI withdrawal: a scoping review and presentation of 85 cases from the Netherlands (Chinchilla et al, 2022) [22]

This was a systematic literature review and analysis of reports of PSSD submitted to the Netherlands Pharmacovigilance Center Lareb.

Literature review summary

The databases PubMed and The Cochrane Library were assessed on 20 October 2020 and 10 November 2020 using the key words 'SSRI prolonged sexual dysfunction', 'SSRI permanent sexual dysfunction', 'PSSD' and 'post SSRI sexual dysfunction'.

A total of 33 studies were included. A summary of the authors findings is outlined in Table 12 below.

**Table 12: Summary of literature review information on PSSD (Chinchilla et al, 2022)**

| Pathophysiology | Presentation | Diagnosis | Treatment |
|---|---|---|---|
| The pathophysiology of sexual dysfunction during SRI treatment can be explained however the mechanisms behind PSSD are still mostly unknown.<br><br>Potential theories<br>*Endocrinal and neurochemical imbalance:* Increase in serotonin causes several neurochemical changes that have roles in sexual response, including prolactin levels, dopamine, oxytocin and testosterone. Not known why levels do not return to normal in some patients after withdrawal.<br><br>*Ion channels:* mechanisms underpinning genital anaesthesia could be associated with transient receptor potential ion channel transduction disturbances.<br><br>*Neurotoxicity*: high levels of serotonin in the peripheral nerves can lead to axonal damage.<br><br>*Epigenetic changes:* SSRIs can trigger epigenetic changes that cause a persistent down regulation of 5-HT1A receptors.<br><br>*Genetic polymorphisms*: genetic polymorphisms in genes related to the glutamatergic system of depressed patients or with structural changes in brain regions involved in sexual response. | Reported in range of ages, sexes and ethnic groups.<br><br>Symptoms<br>• Most reported: loss of libido and sexual drive, erectile dysfunction, week or pleasureless orgasms, genital anaesthesia and anorgasmia.<br>• Most characteristic: genital anaesthesia which is not reported by patients who suffer sexual dysfunction because of depression or another psychological condition.<br><br>Course of symptoms<br>Duration, frequency and intensity of PSSD varies among patients.<br><br>Onset<br>In general, symptoms start after initiation or emerge after withdrawal.<br><br>Impact of PSSD for patients<br>• Emotional burden: affects identity, behaviour and cause a negative self-perception, can cause significant distress.<br>• Social isolation: Affect romantic relationship, loss of jobs<br>• Interaction with healthcare professionals: feel misunderstood, lack of credibility and underestimation of condition | No agreed definition by recognised diagnostic system (e.g DSM, ICD)<br><br>Diagnostic methods used in common practice:<br>• Presence of genital anaesthesia<br>• Checking patient complete history and timeline of symptoms<br>• Use of guidelines for assessing every sexual complaint<br>• Physical assessment to rule out other causes<br>• Assessment of confounding factors such as other conditions, medicines and hormonal imbalances that can also cause sexual dysfunction<br><br>Particular interest should be taken if the patient reports that the sexual dysfunction was absent before the intake of the SRI. | No consensus on the treatment or protocols.<br><br>Possible options:<br><br>*Manipulating the serotonergic and dopaminergic systems*<br>• 5-HT2 or 5-HT3 antagonists (e.g trazadone and mirtazapine)<br>• Dopamine agonists (e.g pramipexole, cabergoline)<br>• 5-HT1 agonist (buspirone)<br><br>*Erectile symptoms*<br>• Phosphodiesterase type 5 inhibitors<br><br>*Non-pharmacological treatment:*<br>• low laser irradiation therapy |

The authors consider there is a priority to raise awareness of PSSD among patients and healthcare professionals.

Healthcare professionals need to provide information about sexual function and record sexual function at baseline, during regular follow ups and after SSRI administration is stopped.

Analysis of spontaneous reports

In the period March 1992 to March 2021, Lareb received 612 reports of sexual dysfunction when using an SSRI.

In 86 reports, patients indicated that they had not recovered from sexual dysfunction even if they had stopped using the SSRI for some time.

These reports included men (n = 54) and women (n = 32). The median age was 32 years (range 14 years to 66 years).

The reporter for 80/86 reports were patients themselves.

Several SSRIs were reported as the causative drug in the reports: paroxetine (n = 28), citalopram (n = 27), fluoxetine (n = 12), sertraline (n = 11), escitalopram (n = 8), and fluvoxamine (n = 2).

Ninety-nine adverse reactions were reported in these 86 reports. Most reported adverse reactions were loss or decrease of libido (n = 53), erectile dysfunction (n = 23), ejaculation disorders (n = 6), anorgasmia (n = 5), nonspecific 'sexual dysfunction' (n = 11) and one case of disturbance in sexual arousal (PGAD).

Symptoms often started within a few weeks after the start of the SSRI.

The median time during which patients had not recovered was 1 year and 4 months after discontinuing their SSRI, based on when they reported to Lareb.

The following quotes were extracted from several spontaneous reports that highlight the major impact on patients:

*"Since starting with the drug paroxetine I have developed severe erectile dysfunction. These complaints have persisted after withdrawal and still persist. I have started a new relationship, but I am very bothered by it. I experience genital numbness and have a severe loss of libido. Before the use of paroxetine I did not have any of these complaints."* (male, 21-30 years)

*"I've only used citalopram for a year, but my sex drive is still close to zero. I have been to a general practitioner and specialists (gynaecologist, sexologist), according to them it is psychological, but I don't believe that. I recovered from the depression and anxiety disorder, but before I started on the medication I enjoyed sex, it was a good outlet and it gave relaxation. The drugs certainly helped in my recovery, but the fact that my libido has not recovered cannot, in my opinion, be explained in any other way than as an ADR of the drugs"* (female, 31-40 years)

*"I was on fluoxetine. The first ADR was loss of sex drive, I remember that so well because I was so amazed about it. Every week thereafter, there was an ADR of the package insert, dry mouth, et cetera. I stopped after about twelve weeks. All ADRs gradually disappeared and the sex drive improved a little, but it was nothing compared with what it had once been"* (male, 41-50 years)

*"I have not been informed about this risk in advance. It is true that sexual feelings could change during use, but not that it can cause permanent damage. I read that it is also an (still) unknown phenomenon. However, I cannot provide any other explanation for this problem. It is thought to be associated with depression. But I've had depression before (without medication) and then my libido was good"* (female, 21-30 years)

**Comments**

The spontaneous reports reviewed in the article identified several cases where patients indicated that their depressive symptoms had recovered or were in remission, but that the sexual symptoms had not yet recovered. In addition, several patients stated that there was no sexual dysfunction before start of treatment. These cases may point towards a medicine cause.

A high percentage of the spontaneous reports in Lareb were reported by patients. While the author did not comment on this finding, it could be possible that these patients did not disclose such symptoms to their healthcare professional. Another possibility could be that healthcare professionals may not be aware of persistent sexual dysfunction as a side effect of SSRIs.

### 3.3.2 Post-SSRI sexual dysfunction: barriers to quantifying incidence and prevalence (Healy & Mangin, 2024) [23]

This article provides a commentary on PSSD based on a combination of academic literature as well as clinical and research experience.

One aspect of the authors discussion is how healthcare professionals do not routinely enquire about the resolution of sexual side effects after stopping an antidepressant and may then be unlikely to discover a case of PSSD unless a patient makes a link themselves.

Another point raised in the article is how it is not uncommon for patients to have difficult experiences with healthcare professionals when trying to seek help for symptoms they suspect are PSSD. Reports of unhelpful, dismissive and hostile responses have been documented in the literature. They include patients having their suspicions ridiculed, being advised to find a different sexual partner, or having their symptoms attributed to something else.

The authors also discuss the presentation of PSSD and how the severity can vary between individuals. Some individuals may not recognise the symptoms, particularly if they see an improvement in symptoms upon treatment discontinuation.

In addition, patients may report general sexual dysfunction symptoms as opposed to specific symptoms that have been associated with PSSD.

The authors conclude that it is not known how many patients, if any, regain their original genital sensation, orgasm intensity and other symptoms.

### 3.3.3 Diagnostic criteria for enduring sexual dysfunction after treatment with antidepressants, finasteride and isotretinoin (Healy et al, 2022) [24]

The authors of this article aim to develop diagnostic criteria for PSSD and persistent genital arousal disorder (PGAD) following SSRI, and in addition for post-finasteride syndrome and post-retinoid syndrome (not discussed in this report).

The criteria were developed using data from two published case series (Hogan et al 2014, and Healy et al 2018) and a multidisciplinary panel of experts.

Significant sexual dysfunction can occur while on treatment and after stopping any SRI medicine. SRIs include SSRIs, SNRIs, SRI tricyclic antidepressants, SRI antihistamines, tetracycline antibiotics such as doxycycline and analgesics like tramadol.

The authors refer to PSSD as a common syndrome happening with any SRI. It is independent of any pre-existing or reactive mental health condition and can be triggered in healthy volunteers after treatment for a few weeks.

Table 13 below outlines the diagnostic criteria developed by the authors for PSSD.

**Table 13: Diagnostic criteria for PSSD adapted from Healy et al 2022**

| Necessary | Additional | Pre-requisites | Ancillary symptoms |
|---|---|---|---|
| Prior treatment with SRI<br><br>An enduring change in somatic (tactile)[a] or erogenous (sexual)[b] genital sensation after treatment stops. | Enduring reduction or loss of sexual desire<br><br>Enduring erectile dysfunction (males)<br><br>Enduring inability to orgasm or decreased sensation of pleasure during orgasm<br><br>The problem is present for ≥ 3 months after stopping treatment | No evidence of pre-treatment sexual dysfunction that matches the current profile<br><br>No current medical conditions, medicines or substance abuse that could account for the symptoms | Sexual symptoms: genital pain, reduced nipple sensitivity, decreased or loss of nocturnal erections (males), reduced ejaculatory force (males), flaccid glans during erection (males), decreased vaginal lubrication (females).<br><br>*Non-sexual symptoms:* emotional numbing, depersonalization, other sensory problems involving skin, smell, taste or vision, cognitive impairment. |

A. Enduring change in somactic (tactile) genital sensation: genitals feels like they were exposed to an anaesthetic.
B. Enduring change in erogenous (sexual) genital sensation: genital touch fells like being touched on any other body part.

The authors comment PSSD can vary in severity. A patient may regain the ability to achieve orgasm upon discontinuing treatment, but the orgasm no longer feels the same as pre-treatment. Any severity of symptoms should be classified as PSSD if there hasn't been a full return to pre-treatment baseline.

The article also considers implications for children exposed to SSRI, and that given how sexual side effects may develop before sexual maturity, the person may have no pre-treatment baseline for comparison. Therefore, it may be difficult to recognise symptoms such as low sexual desire, reduced genital sensation and pleasureless orgasm.

## 3.4 New Zealand spontaneous case reports

### 3.4.1 Sexual dysfunction reports

Up to 11 May 2026, there have been 65 reports of sexual dysfunction (identified using the MedDRA SMQ 'sexual dysfunction') for SSRIs and 20 reports for venlafaxine. An overview of these reports is provided below.

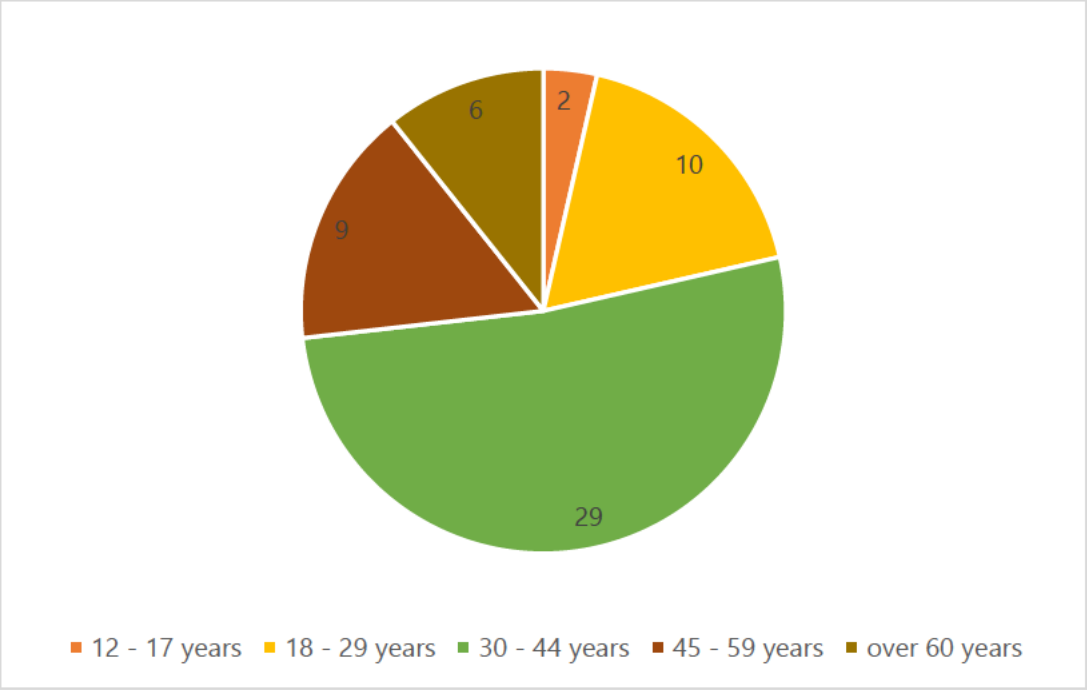
*3.4.1.1 SSRIs*

[redacted] Most reports were for males (58%).

[redacted]

Figure 2 outlines the age range for the reports where age is known (n=56). Approximately 50% of the reports were in individuals aged between 30 – 44 years of age.

**Figure 2: New Zealand case reports, SSRIs and sexual dysfunction (MedDRA SMQ), by age range (n=56)**

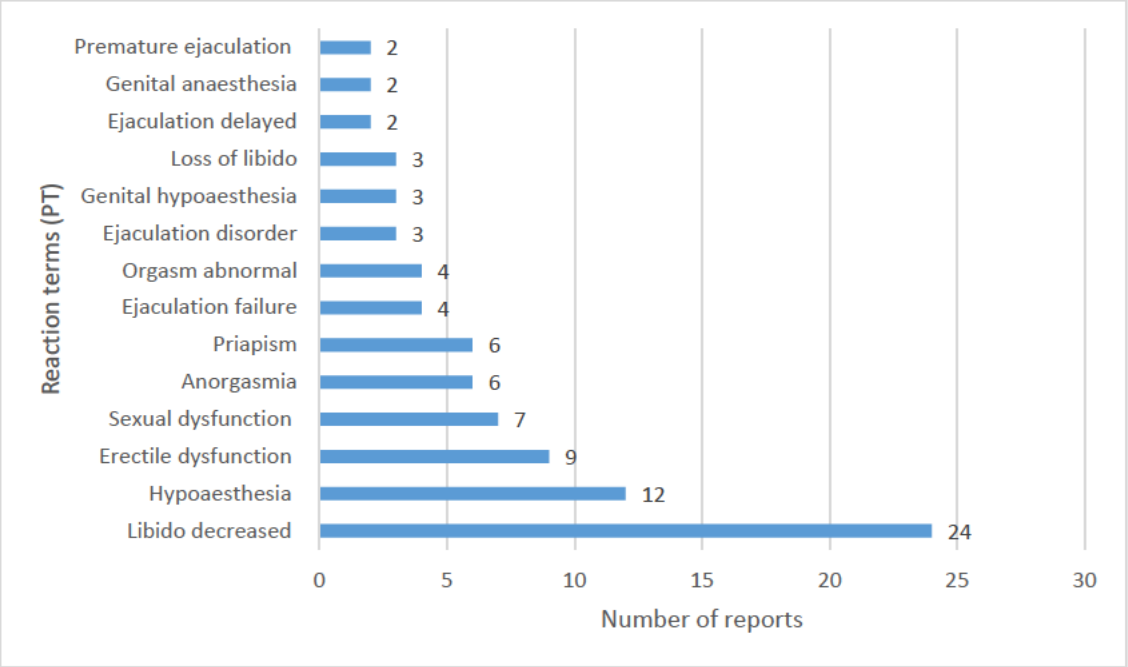



The most frequently reported SSRI was citalopram (35%), followed by fluoxetine (29%), paroxetine (17%), sertraline (14%) and escitalopram (5%).

[redacted]

Figure 3 below highlights the most frequently reported reaction PTs from the 65 reports. Note that one report may include more than one reaction, therefore the total number of reactions is higher that the number of reports.

**Figure 3: New Zealand case reports, SSRIs and sexual dysfunction (MedDRA SMQ), by most reported reaction PT**




[redacted] These reports may suggest long-lasting sexual side effects.

**Comments**

[redacted]

Considering usage data for these medicines (section 2.1.2), the number of spontaneous reports related to sexual dysfunction may appear to be low. It is possible reporting of such reactions with SSRIs are underreported given the nature of the side effects.

[redacted] Some of these cases could potentially be PSSD. Further information about PSSD/possible PSSD cases is discussed below.

*3.4.1.2 SNRIs*

[redacted] Most reports were in males (60%).

[redacted]

Where age was reported, most reports were in those aged 45 – 59 years (9 reports), followed by those aged 30 – 44 years (6 reports) and 3 reports were in those aged 18 – 29 years of age.

[redacted]

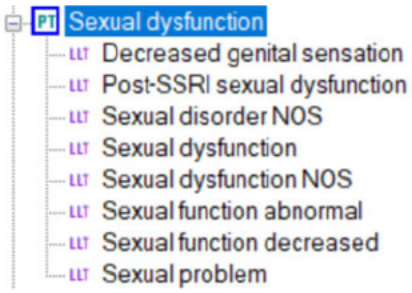
The most reported PTs under the SMQ 'sexual dysfunction' were libido decreased (11 reports), erectile dysfunction (5 reports) and hypoesthesia (3 reports).

[redacted]

### 3.4.2 PSSD/possible PSSD case reports

These cases were identified in the database as follows:

The MedDRA code for PSSD was added in 2021 as a LLT mapped to the PT 'sexual dysfunction'.




Within New Zealand spontaneous case reports, cases of PSSD and possible cases of PSSD were identified from the datasets outlined above.

Cases included were those coded with:

- LLT 'post-SSRI sexual dysfunction'
- Stop date of treatment available and/or when action taken with medicine is 'drug withdrawn' plus outcome of the report was 'not recovered/not resolved/ongoing'.

Cases where it was unclear from the information provided if the medicine was stopped and symptoms continued were excluded.

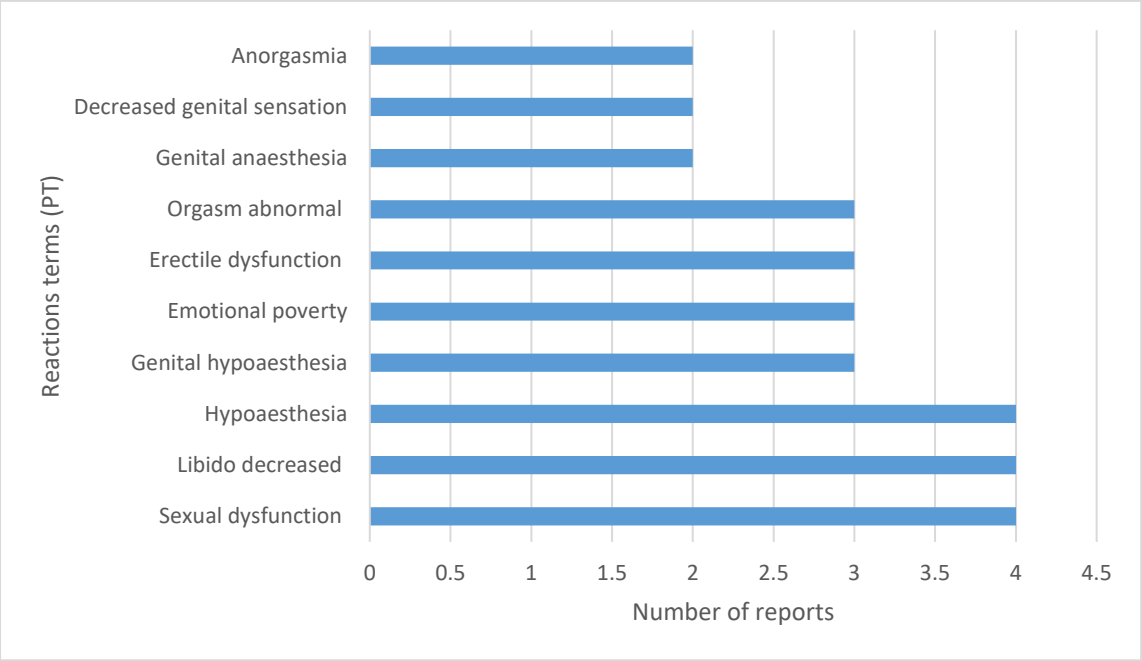
Due to the nature of spontaneous reporting, some reports may have too limited information for them to be identified as possible PSSD. Therefore, it is possible that not all cases of possible PSSD have been identified.

This search for cases of PSSD and possible cases of PSSD focused on sexual related symptoms. Nonsexual symptoms may also have been reported.

#### *3.4.2.1 SSRIs*

[redacted]

**Figure 4: New Zealand case reports, SSRIs and PSSD/possible PSSD cases, by most reported reaction PT**




Further details of the reports are presented in the Table 14 below. See also Annex 1.

**Table 14: New Zealand spontaneous case reports – PSSD/possible PSSD**

| Report ID | [redacted] | Sex | Age | Medicine | Reactions (PTs) | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|---|---|---|---|
| NZ-Medsafe-160415 | [redacted] | Unknown | Not reported | escitalopram | Emotional poverty | [redacted] | [redacted] | [redacted] |
| | | | | | Genital anaesthesia | [redacted] | | |
| | | | | | Loss of libido | [redacted] | [redacted] | [redacted] |
| | | | | | Male orgasmic disorder | [redacted] | [redacted] | |
| | | | | | Mental impairment | [redacted] | [redacted] | [redacted] |
| | | | | | Premature ejaculation | [redacted] | | |
| | | | | | Sexual dysfunction [redacted] | [redacted] | | |
| | | | | | Urinary incontinence | [redacted] | | |
| | | | | | Urine flow decreased | [redacted] | | |
| NZ-Medsafe-162162 | [redacted] | Female | 18 | citalopram | Sexual dysfunction [redacted] | [redacted] | [redacted] | [redacted] |
| NZ-Medsafe-162555 | [redacted] | Female | 17 | citalopram | Abnormal dreams | [redacted] | [redacted] | [redacted] |
| | | | | | Alcohol intolerance | [redacted] | | |
| | | | | | Apathy | [redacted] | | |
| | | | | | Aphasia | [redacted] | | |
| | | | | | Bladder pain | [redacted] | | |
| | | | | | Breast swelling | [redacted] | | |
| | | | | | Cognitive disorder | [redacted] | | |
| | | | | | Deafness | [redacted] | | |

| Report ID | [redacted] | Sex | Age | Medicine | Reactions (PTs) | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|---|---|---|---|
| | | | | | Dissociation | | | |
| | | | | | Disturbance in attention | | | |
| | | | | | Dysphagia | | | |
| | | | | | Emotional poverty | | | |
| | | | | | Hallucination | | | |
| | | | | | Hypoaesthesia | | | |
| | | | | | Irritable bowel syndrome | | | |
| | | | | | Menstrual headache | | | |
| | | | | | Misophonia | | | |
| | | | | | Nervous system disorder | | | |
| | | | | | Peritonitis | | | |
| | | | | | Photophobia | | | |
| | | | | | Pollakiuria | | | |
| | | | | | Sexual dysfunction [redacted] | | | |
| | | | | | Sleep disorder | | | |
| | | | | | Sleep paralysis | | | |
| | | | | | Social problem | | | |
| | | | | | Suicidal ideation | | | |
| | | | | | Upper-airway cough syndrome | | | |

| Report ID | [redacted] | Sex | Age | Medicine | Reactions (PTs) | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|---|---|---|---|
| NZ-Medsafe-163411 | [redacted] | Male | 44 | citalopram | Ejaculation disorder<br>Erectile dysfunction<br>Libido decreased | [redacted] | [redacted] | [redacted] |
| NZ-Medsafe-158524 | [redacted] | Male | 29 | sertraline | Emotional poverty<br>Genital hypoesthesia<br>Loss of libido<br>Withdrawal syndrome | [redacted] | [redacted] | [redacted] |
| NZ-Medsafe-154169 | [redacted] | Male | 36 | fluoxetine | Alcohol problem<br>Anorgasmia<br>Cognitive disorder<br>Erectile dysfunction<br>Fatigue<br>Genital anaesthesia<br>Hypoaesthesia<br>Infertility<br>Loss of libido | [redacted] | [redacted] | [redacted] |
| NZ-Medsafe-154868 | [redacted] | Male | 30 | paroxetine | Genital hypoesthesia<br>Orgasm abnormal | [redacted] | [redacted] | [redacted] |

| Report ID | [redacted] | Sex | Age | Medicine | Reactions (PTs) | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|---|---|---|---|
| | | | | | Sexual dysfunction [redacted] | | | |
| **NZ-Medsafe-159428** | [redacted] | Male | Not reported | sertraline | Cognitive disorder<br>Dizziness<br>Feeling hot<br>Genital hypoesthesia<br>Headache<br>Memory impairment<br>Nausea<br>Orgasm abnormal<br>Sexual dysfunction [redacted]<br>Speech disorder | | [redacted] | [redacted] |
| **147868** | [redacted] | Male | 37 | sertraline | Dizziness<br>Gastrointestinal disorder<br>Lethargy<br>Libido decreased<br>Yawning | | [redacted] | [redacted] |

| Report ID | [redacted] | Sex | Age | Medicine | Reactions (PTs) | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | | |
| **148018** | [redacted] | Male | 23 | sertraline | Erectile dysfunction<br>Fatigue<br>Libido decreased<br>Withdrawal syndrome | [redacted] | [redacted] | [redacted] |
| **138298** | [redacted] | Female | 29 | sertraline | Anorgasmia<br>Libido decreased | [redacted] | [redacted] | [redacted] |
| **096579** | [redacted] | Female | 32 | citalopram | Formication<br>Hypoaesthesia<br>Paraesthesia | [redacted] | [redacted] | [redacted] |
| **091279** | [redacted] | Female | 81 | fluoxetine | Orgasm abnormal | [redacted] | [redacted] | [redacted] |

| Report ID | [redacted] | Sex | Age | Medicine | Reactions (PTs) | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|---|---|---|---|
| 067563 | [redacted] | Female | 60 | citalopram | Abdominal pain<br>Hyperhidrosis<br>Hypoaesthesia<br>Product use issue<br>Therapeutic response decreased | [redacted] | [redacted] | [redacted] |

[redacted]

Medsafe/CARM have received several reports where PSSD has been reported. In addition, on review of reports of sexual dysfunction with SSRIs, reports of continued symptoms or new symptoms after treatment discontinuation were identified.

All reports reviewed (14) included that the symptoms are persisting. At the time of reporting for some of the reports, the symptoms had been present for several years.

Genital anaesthesia/genital hypoesthesia was reported in several cases that also reported PSSD or were identified as possible PSSD. This aligns with the diagnostic criteria proposed by Healy et al 2022. Experiencing changes in genital sensation while on treatment with an SSRI could possibly point to risk of PSSD.

Hypoesthesia was a commonly reported symptom. It was unclear if this also included genital hypoesthesia.

Emotion blunting/lack of emotions, a non-sexual symptom associated with PSSD, was reported by several individuals.

Most cases were reported recently (2024/2025), which may suggest that awareness of PSSD is increasing and/or has been given increased recognition as a syndrome of itself.

[redacted]

Limitations with spontaneous reporting are acknowledged including missing information, confounding and other causes of the symptoms.

*3.4.2.2 SNRIs*

Cases were excluded where the reporter had submitted the report at, or just after, the time of discontinuation. While it was reported that the symptoms were mostly improving, the presence of long-lasting symptoms in these cases was not known.

Apart from one report, there was insufficient information to identify any possible PSSD cases from the reports with PTs under SMQ 'sexual dysfunction' for venlafaxine. Further details of this report are listed in Table 15 below.

**Table 15: New Zealand spontaneous case reports, PSSD/possible PSSD – SNRIs**

| Report ID | [redacted] | Sex | Age | Medicine | Reactions (PTs) | [redacted] | [redacted] | [redacted] |
|---|---|---|---|---|---|---|---|---|
| 130193 | [redacted] | Male | 56 | Venlafaxine [redacted] | Libido decreased<br>Pollakiuria | [redacted] | [redacted] | [redacted] |

[redacted]

[redacted]

# 4 International regulators

## 4.1 Regulatory action

The information below presents regulatory action from 2020 onwards.

### 4.1.1 Patient and family experiences inform antidepressant safety information review (Medicines and Healthcare products Regulatory Agency, 2025) [1]

An expert working group of the Commission on Human Medicines (CHM) advising the Medicines and Health Products Regulatory Agency (MHRA), concluded a detailed review on how the potential risks associated with 28 antidepressant medicines are communicated within the patient information leaflets (PIL).

The review was launched after concerns were raised by families and patients that current safety warnings in PILs for these medicines did not clearly explain certain side effects, specifically suicidal behaviours and sexual dysfunction, that may continue after the treatment is stopped.

Based on the group's recommendations, the CHM advised that the wording in the PILs should be strengthened.

### 4.1.2 Updated warnings about persistent sexual dysfunction for antidepressants (Therapeutic Goods Administration (TGA), 23 May 2024) [25]

The TGA published a Safety Update about product information (PI) for SSRIs and SNRIs being aligned so that the warning about sexual dysfunction persisting after discontinuation was included in the relevant PIs.

The following information was aligned across the relevant PIs:

***4.4 Special warnings and precautions for use:***

*Sexual dysfunction*

*Selective serotonin reuptake inhibitors (SSRIs)/serotonin norepinephrine reuptake inhibitors (SNRIs) may cause symptoms of sexual dysfunction (see section 4.8). There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRI.*

Other information in the safety update:

- Sexual dysfunction effects can persist for weeks to years and significantly harm patient's quality of life.
- Persistent sexual dysfunction after treatment is stopped is thought to be rare. However, these symptoms are likely to be under-reported and their prevalence is not known.
- Health professionals should be alert to this issue and consider if current or previously antidepressant use could be a factor in patients reporting sexual dysfunction.

At the time when the safety reported was published, the TGA had received 89 reports describing sexual dysfunction with an SSRI or SNRI to their Adverse Event Management System database (to April 2024).

Of these, 4 described persistent sexual dysfunction after treatment was stopped. The 3 men and 1 woman ranged in age from 18 to 42. Reported symptoms included difficulty reaching orgasm, weakened orgasms, erectile dysfunction and reduced penile sensation. The effects persisted for 12 months to 3.5 years.

### 4.1.3 Summary safety review - SSRIs/SNRIs – Assessing the potential risk of sexual dysfunction despite treatment discontinuation – Health Canada, 2021 [26]

In 2021, 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 review was triggered by the EMA, which had been 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.

Health Canada reviewed information from published and unpublished epidemiological studies and case reports from individual patients. Epidemiological 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. Because of concerns about the accuracy of their findings, these were therefore not included.

The review focused on case reports. 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).

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 dysfunction despite discontinuation of SSRIs/SNRIs.

# 5 DISCUSSION AND CONCLUSIONS

Depression is a common mental health condition, of which SRIs are pharmacological treatment options. Sexual dysfunction with SSRIs/SNRIs is a commonly experienced side effect.

Data sheets for SSRIs/SNRIs include a warning stating that symptoms of sexual dysfunction may occur on treatment and that there have been reports of long-lasting sexual dysfunction where the symptoms have continued despite treatment discontinuation. Specific sexual side effects are listed in section 4.8.

Overtime, the awareness and recognition of the presence of long-lasting sexual side effects following SSRI/SNRI discontinuation has increased. PSSD is widely used within the literature to describe this syndrome.

The term PSSD is not listed as a side effect or included in sexual dysfunction warnings in prescribing information internationally, however, is recognised as a MedDRA LLT term (since 2021).

Available data on PSSD mainly comes from case reports, surveys and retrospective chart reviews. Several observational studies took place in males only, and in those with PSSD (self-reported in survey studies). The prevalence of PSSD in people who take SSRIs and SNRIs is not possible to estimate from available data sources.

It appears more data is available for SSRIs. While PSSD specifically includes 'SSRIs' in its name, it is seen to group both SSRIs and SNRIs together as SRIs. PSSD may extend to other medicines with serotonin activity that are not used as antidepressants such as tramadol.

The mechanisms for PSSD are not well understood. Possible theories for the continuation of symptoms despite treatment discontinuation include that receptor levels may not return to pre-treatment state or permanent structural changes in erectile tissue may occur.

Within the literature, PSSD appears to be reported more in males than females and in younger individuals (around 30 years of age). Symptoms are generally severe and long-lasting. However, the spontaneous reporting data is more balanced.

Not all individuals who experience sexual side effects with SSRIs/SNRIs experience PSSD. Potential risk factors for PSSD are not clear.

PSSD in the literature is characterised by several symptoms (both sexual and non-sexual) that may occur during treatment and continue/worsen after discontinuation or occur following treatment discontinuation only. There is variability in the symptoms present, onset and severity between individuals. Such factors may also change over time; however, some individuals reported that they had not regained previous functions.

The most frequent PSSD symptoms reported were sexual related (effects on libido, effects on orgasm, changes in genital sensation and ED (males)). Non-sexual symptoms such as lack of emotions and body numbness may also occur but possibly less often. In 2 studies in males with PSSD, physical assessment of ED and genital number found abnormalities.

Genital numbing (genital hypoesthesia, genital anaesthesia) is commonly referred to as a main symptom of PSSD. Criteria developed by Healy at al 2022, list this symptom as necessary for diagnosis. Genital numbness is not considered to be a symptom of sexual dysfunction related to depression or other mental health conditions.

Many case reports and individuals with PSSD in studies report experience of changes in genital sensation. [redacted]

Experiencing sexual dysfunction can negatively affect an individual's quality of life. Case reports in individuals with PSSD detail significant impacts to their wellbeing.

Standardised guidelines for diagnosis for PSSD are not available. However, PSSD may be suspected in individuals who have been on SRIs and who did not have any sexual dysfunction symptoms prior to treatment and where no other causes are identified. In addition, when an appropriate time has passed after discontinuation.

A concern has been raised in the literature about the use of these medicines in children and how their future sexual function may be impacted.

Medsafe/CARM have received several reports where individuals have experienced ongoing or new sexual +/- nonsexual symptoms following discontinuation of SRIs, particular with use of SSRIs. [redacted]

It is important that healthcare professionals enquire about sexual side effects with SSRIs/SNRIs, including asking about specific symptoms. Enquiring about symptoms after discontinuing treatment may discover cases of PSSD that may not have been detected otherwise.

In the data sheets for SSRIs/SNRIs, information on possible symptoms and general advice to healthcare professionals, such as monitoring recommendations, is not included. Whereas this information is included in FDA labels. Therefore, depending on the Committee's opinion on the evidence for PSSD the information in the data sheets may need to be updated.

# 6 ADVICE SOUGHT

The Committee is asked to advise:

- Whether for sexual dysfunction with SSRIs/SNRIs (in general), is the current information in the data sheets sufficient to manage this risk? If no, what updates are needed?
- On the strength of the evidence for an association between SRIs and the syndrome post-SSRI sexual dysfunction (PSSD) whether the evidence warrants updates to the data sheets for SRIs.
- Whether any communication is required other than in MARC's remarks?

# 7 ANNEXES

Annex 1: New Zealand Spontaneous case Reports

# 8 REFERENCES

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