

## Summary Safety Review - Tramadol-containing products - Assessing the Potential Risk of Hallucinations

**Product:** Tramadol-containing products

**Potential Safety Issue:** Hallucinations, such as seeing or hearing things that are not there

### Key Messages

- **Tramadol-containing products are authorized for sale in Canada to treat moderate to moderately severe pain in adults who require treatment for several days or more.**
- **Health Canada reviewed the risk of hallucinations with the use of tramadol-containing products. This review was triggered by an increase in the number of reported cases (Canadian and international) of hallucinations in patients treated with these products.**
- **Health Canada's review of the available information has established a link between the use of tramadol-containing products at normal doses and the risk of seeing or hearing things that are not there (visual and auditory hallucinations), particularly in patients over 65 years of age.**
- **Health Canada will work with manufacturers to update the Canadian product safety information for tramadol-containing products to include the risk of visual and auditory hallucinations at normal doses, including a higher risk in patients over 65 years of age.**

### Overview

Health Canada reviewed the risk of hallucinations with tramadol-containing products. The safety review was triggered by information submitted from a manufacturer showing an increase in the number of reported cases (Canadian and international reports) of hallucinations with tramadol use at normal doses.

### Use in Canada

- Tramadol-containing products are prescription drugs authorized for sale in Canada to treat moderate to moderately severe pain in adults who require treatment for many days or more.
- Tramadol has been marketed in Canada since 2005 and is available alone or in combination with acetaminophen. It is marketed under the brand names Zytram XL, Tridural, Ralivia, Ultram, Durela and Tramacet. Generic versions of tramadol-containing products are also available for sale in Canada.
- Tramadol-containing products are available as immediate release and controlled release tablets or capsules. The immediate release formulations are available in strengths of 37.5 mg (in combination with 325 mg of acetaminophen) and 50 mg tramadol hydrochloride alone. Extended and controlled release formulations are available at doses ranging from 100 to 400 mg tramadol hydrochloride.
- There were about 1.6 million tramadol prescriptions filled in Canada in 2019, a 4% increase compared to 2015. Tramadol prescriptions have been steadily increasing over the last few years, especially for patients over 65 years of age.

## Safety Review Findings

- Health Canada reviewed the available information from searches of the Canada Vigilance database<sup>a</sup>, international databases, scientific and medical literature as well as information received from one of the manufacturers.
- At the time of the review, Health Canada had received 54 Canadian reports of hallucinations related to the use of tramadol-containing products. Of the 54 Canadian reports, only 2 met the criteria for further assessment to determine if there was a link between the use of tramadol and hallucinations. The remaining 52 reports could not be assessed due to several contributing factors such as incomplete information in the reports, or the patients were taking other medications at the same time that may have contributed to this risk.
- Health Canada reviewed 24 serious case reports (2 Canadian and 22 international) of hallucinations with the use of tramadol-containing products. Of the 24 case reports, 1 case (an elderly patient) was found to be probably linked, 18 cases (including 2 Canadian cases) were possibly linked, with 11 of these 18 cases involving elderly patients, 1 case was not likely to be linked, and 4 cases did not have enough information to be assessed.
- Health Canada also assessed a review from the published scientific literature that included 101 cases of hallucinations with the use of tramadol. Most reported hallucinations were visual and/or auditory and occurred in patients older than 65 years of age. Health Canada's review of the published study supported a possible link between hallucinations and tramadol use.

## Conclusions and Actions

- Health Canada's review of the available information has established a link between the use of tramadol-containing products, at normal doses, and the risk of visual and auditory hallucinations, especially in patients over 65 years of age.
- Health Canada will work with manufacturers to update the Canadian product safety information for tramadol products to include the risk of visual and auditory hallucinations at normal doses, including a higher risk in patients over 65 years of age.
- Health Canada will continue to monitor safety information involving tramadol-containing products, as it does for all health products on the Canadian market, to identify and assess potential harms. Health Canada will take appropriate and timely action should any new health risks be identified.

## Additional Information

The analysis that contributed to this safety review included scientific and medical literature, Canadian and international information, and what is known about the use of tramadol-containing products both in Canada and internationally.

For additional information, [contact the Marketed Health Products Directorate](#)

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<sup>a</sup> Canadian reports can be accessed through the [Canada Vigilance Online Database](#).