

## **Summary Safety Review – Methadone-Containing Products Used to Treat Opioid Dependence – Assessing the Potential Risk of Lack of Effect when Switching between Different Products**

**Product:** Methadone-containing products used to treat opioid dependence

**Potential Safety Issue:** Lack of effect when switching between different methadone products used for the treatment of opioid dependence

### **Key Messages**

- **Some methadone-containing products are authorized in Canada for use in opioid dependent patients requiring substitution treatment to prevent side effects developed when these patients stop using other opioids (opioid withdrawal symptoms).**
- **Health Canada reviewed the risk of lack of effect after receiving reports from Canadian healthcare professionals and patients suggesting that some patients experienced symptoms of opioid withdrawal after being switched from one methadone-containing product to another.**
- **A safety review completed by Health Canada has found that there may be a link between switching methadone-containing products used to treat opioid dependence and the risk of lack of effect, which may present as withdrawal symptoms. Patients experiencing withdrawal symptoms need to be seen often by their healthcare professional and may need an adjustment in the dose of methadone.**
- **Health Canada will be working with the manufacturers to update the Canadian product safety information to warn of this potential safety issue.**

### **Overview**

- Health Canada reviewed the potential risk of lack of effect, which may present as drug withdrawal, with methadone-containing products used to treat opioid dependence. The review was triggered by recent reports received from Canadian patients and healthcare professionals suggesting that some patients experienced symptoms of opioid withdrawal after being switched from one methadone product to another.

### **Use in Canada**

- Methadone-containing products used to treat opioid dependence have been available in Canada since the 1960s. Methadone hydrochloride oral solution (1 mg/mL) and methadone hydrochloride oral concentrate (10 mg/mL) products prepared by the manufacturers and used to treat opioid dependence in adults have been marketed in Canada since 2001 under the brand names Metadol-D, Methadose, and Sandoz Methadone. Jamp Methadone Oral Concentrate and Odan-Methadone have also been

authorized for use in Canada since January 2020, as of the date of this communication, they are not marketed. Methadone powder is also available to pharmacists to make (compound) their own methadone solutions. After being mixed with a flavoured liquid, these products are dispensed to patients and taken by mouth (orally).

- There were about 13 million prescriptions filled in 2019 for methadone-containing products used to treat opioid dependence.

### **Safety Review Findings**

- Health Canada reviewed the scientific and medical literature, Canadian and international information including case reports in the Canada Vigilance<sup>a</sup> as well as information received from manufacturers, Canadian healthcare professionals and patients.
- Health Canada's review looked at 22 Canadian reports (12 from the Canada Vigilance database and 10 provided by the manufacturers) linked with a lack of effect of methadone-containing liquid products (taken orally) used to treat opioid dependence.
- These reports suggested that these methadone-containing products did not work as well to ease withdrawal symptoms and patients who had generally been on stable methadone treatment for a long time, as they reported experiencing withdrawal symptoms after being switched from one methadone product to another. Assessing whether the lack of effect was specifically related to one methadone-containing product and why the withdrawal symptoms happened was challenging due to lack of information. However, a link between methadone-containing products used for opioid dependence and lack of effect could not be ruled out in these cases.
- The Department also contacted over 40 Canadian healthcare professionals, professional associations and patient treatment centers in order to gather feedback regarding this safety issue from healthcare professionals and patients. In total, 7 responses were received (5 from healthcare professionals and 2 from patients). The 5 responses received from healthcare professionals reported changes in how patients responded to the treatment for opioid drug dependence after being switched from one methadone-containing product to another. The problem was fixed by increasing the dose of the methadone-containing product they were taking, by switching to a new methadone-containing product, or by switching back to the original methadone-containing product. One of the 2 patient responses also described that the new methadone-containing products were not working as well as the old one.
- Health Canada also assessed 5 published studies found in the Canadian scientific literature discussing the issue of lack of effect when patients treated for opioid dependence in British Columbia (Canada) were switched from one methadone-containing product to another. These studies generally found that some patients did worse following a product change. However, the studies did not identify specific causes for the observed lack of effect.

- Canadian and international literature, as well as feedback from Canadian healthcare professionals, suggest that psychosocial factors may play a role and some patients do not tolerate methadone-containing product changes.
- While the cause has not been linked to any specific problem with the methadone-containing product used following a switch, withdrawal symptoms can be serious and patients should consult with their healthcare professional if they have concerns about switching products or if they experience withdrawal symptoms.

### **Conclusions and Actions**

- Health Canada's review found there may be a link between methadone and the risk of lack of effect, which may present as drug withdrawal, when switching between methadone-containing products, although the reason for this is unclear. Patients experiencing withdrawal symptoms need to be seen often by their health care professional and may need an adjustment in the dose of methadone.
- Health Canada will be working with manufacturers to update the Canadian product information to warn of this potential safety issue.
- Health Canada encourages consumers and healthcare professionals to [report](#) any side effects related to the use of methadone or other health products.
- Health Canada will continue to monitor safety information involving methadone, 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 if and when any new health risks are 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 methadone used to treat addiction to opioids both in Canada and internationally.

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

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- a. Canadian reports can be accessed through the [Canada Vigilance Online Database](#).