

Summary Safety Review – METHADOSE and METADOL-D - Assessing the potential risk of serious harm in children exposed to methadone through breast milk

Product: Methadose, Metadol-D (methadone hydrochloride)

Potential Safety Issue: Risk of serious harm (including death) in children breastfed by mothers in methadone treatment

Key Messages

- Methadose and Metadol-D are methadone-containing drugs used to treat addiction to opioids (such as heroin) in adults. They work to prevent withdrawal symptoms, which are side effects caused by stopping the use of other opioids.
- Health Canada became aware of a published article¹ that reported 2 Canadian cases of death in children who had increased levels of methadone in their blood because they were being breastfed by mothers in treatment programs for opioid addiction (methadone maintenance programs).
- Health Canada's review of the available information found that there may be a link between methadone and the risk of serious harm (including death) in children exposed through breast milk. Health Canada will be working with the manufacturers of Methadose and Metadol-D to strengthen the existing product information to specifically include the risk of serious harm, including death, in children exposed to methadone through breast milk.

Overview

Health Canada reviewed this safety issue because a published article reported 2 Canadian cases of death in children who had methadone in their blood because they were breastfed by mothers in methadone maintenance programs for opioid addiction.

Small amounts of methadone can be passed to children through breast milk. Canadian and international treatment guidelines for opioid addiction encourage breastfeeding by mothers in methadone maintenance programs, although both mothers and children should be closely monitored². The benefits and risks of breastfeeding during methadone maintenance treatment should be carefully considered.

Reports of serious side effects including death are very rare in children who were being breastfed by mothers in methadone maintenance programs.

Use in Canada

- Methadose (Methadone Hydrochloride Oral Concentrate) and Metadol-D (Methadone Hydrochloride Tablets, Oral Solution and Concentrate) are authorized for sale in Canada to treat opioid addiction in adults.
- Methadone is a synthetic opioid and is considered a controlled narcotic substance that is available only by prescription.
- Methadose and Metadol-D have been marketed in Canada since 2013 and 2014 respectively.
- There were about 11 million prescriptions for Methadose and Metadol-D filled in Canada in 2017.

Safety Review Findings

- At the time of the review, there were only 2 Canadian cases^a of methadone toxicity in children exposed through breast milk, both of which involved death. Both reports were found to have a possible link between methadone and serious harm (including death) in children exposed through breast milk.
- This safety review also looked at 13 international cases of methadone toxicity in children exposed through breast milk, 10 of which involved death. A possible link between methadone and the risk of serious harm (including death) in children exposed through breast milk was found in 12 of these cases. The remaining case did not have enough information to be assessed.
- Small amounts of methadone can be passed to children through breast milk and breastfeeding may, in very rare cases, put children at risk of serious side effects including trouble breathing (severe respiratory depression), heart problems and death.
- It is possible that genetic factors may be a reason why some children are more sensitive to the effects of methadone than others, but these genetic factors are not well understood. Genetic testing in 2 of the cases involving death suggested that the children may have been especially sensitive to the effects of methadone.
- Scientific literature and various Canadian and international guidelines encourage breastfeeding among mothers maintained on methadone. However, the benefits and risks of breastfeeding during methadone maintenance treatment should be carefully considered.
- In all cases that were reviewed, there were factors that made assessment of the cases difficult. These included lack of information about the mother's methadone dose, cause of death, and medical history or drug use that may have contributed to the serious side effects.
- The product information for Methadose and Metadol-D advises caution when methadone is used to treat nursing women. For both products, the product information notes that the

benefits and risks of breastfeeding while on methadone therapy should be carefully weighed and that breastfeeding mothers and their children should be monitored closely.

- The European Medicines Agency and the United States Food and Drug Administration both have similar product information listing the risk of serious harm to children who are exposed to methadone through breast milk.

Conclusions and Actions

- Health Canada's review of the available information found that there may be a link between methadone and the risk of serious harm (including death) in children breast fed by mothers in methadone treatment.
- Health Canada will be working with the manufacturers of Methadose and Metadol-D to strengthen their product information to warn of the risk of serious harm, including death, in children exposed to methadone through breast milk.
- Health Canada encourages consumers and healthcare professionals to report any side effects related to the use of these 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 adverse reaction reports, and what is known about the use of this drug both in Canada and internationally.

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

References

- 1 Madadi P, Kelly L, Ross C, Kepron C, Edwards J, Koren G. Forensic Investigation of Methadone Concentrations in Deceased Breastfed Infants. *Journal of Forensic Sciences*. 2016;61:1-5
- 2 College of Physicians and Surgeons of Ontario: Methadone Maintenance Treatment Program Standards and Clinical Guidelines <https://www.cpso.on.ca/uploadedFiles/members/MMT-Guidelines.pdf> (consulted on February 2, 2018)

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