

# Health Canada advisory on domperidone

*Should I avoid prescribing domperidone to women to increase milk production?*

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### Abstract

**Question** I often prescribe domperidone to women as a galactagogue starting at a dose of 30 mg and increasing the dose as needed. In March of this year, Health Canada released an advisory warning of domperidone use and abnormal heart rhythms and sudden cardiac death. Should I cap doses at 30 mg or stop prescribing domperidone all together to these women?

**Answer** The Health Canada warning is based on 2 studies. The results of the studies are not directly applicable to breastfeeding and should not change the way you normally manage otherwise healthy breastfeeding women.

### Avis de Santé Canada sur la dompéridone

*Devrais-je éviter de prescrire de la dompéridone aux femmes pour augmenter la production de lait?*

### Résumé

**Question** Je prescris souvent de la dompéridone aux femmes comme galactagogue, en commençant par une dose de 30 mg et en augmentant cette dose au besoin. En mars cette année, Santé Canada a publié une mise en garde concernant l'utilisation de la dompéridone et les risques d'anomalies graves du rythme cardiaque et de mort subite. Devrais-je limiter les doses à 30 mg ou arrêter complètement de prescrire de la dompéridone à ces femmes?

**Réponse** L'avis de Santé Canada se fonde sur 2 études. Les résultats de ces études ne sont pas directement applicables à l'allaitement maternel et ne devraient pas changer la façon dont vous prenez normalement en charge les femmes autrement en bonne santé qui allaitent.

Domperidone is a dopamine antagonist with anti-emetic and gastroprokinetic properties.<sup>1</sup> It is indicated for the symptomatic management of upper gastrointestinal motility disorders and gastrointestinal symptoms associated with the use of dopamine agonist antiparkinsonian agents.<sup>1</sup>

Breastfeeding is recommended for all infants, with very few exceptions, as there are many benefits for the developing child, including evidence for improved cognitive development, reduced incidence of infection, and less risk of sudden infant death syndrome.<sup>2</sup> Further, there is evidence of benefits for the mother, such as reduced incidence of reproductive cancers.<sup>3</sup> Some women, however, experience insufficient breast milk production. Domperidone has been demonstrated to induce and maintain lactation by increasing prolactin levels.<sup>4</sup> A recent systematic review and meta-analysis by Motherisk demonstrated a statistically significant increase of 74.7% (95% CI 54.6 to 94.9,  $P < .001$ ) in daily milk production following treatment with domperidone and found no maternal safety issues when compared with placebo.<sup>5</sup> At present, some intervention trials are under way to define the appropriate dose in specific populations (eg, mothers of preterm

infants). Only minimal amounts of domperidone are excreted into breast milk (less than 0.1% of the maternal weight-adjusted dose), and side effects in breastfed infants have not been reported.<sup>3,6-8</sup> Therefore, when nonpharmacologic treatments fail or are inadequate, domperidone might be an option.

### Health Canada advisory

In March 2012 Health Canada released an advisory to health care professionals and to the public warning of possible serious side effects associated with the use of domperidone.<sup>9,10</sup> The warning was based on 2 studies reporting an association of domperidone with serious abnormal heart rhythms and sudden cardiac death (SCD).<sup>11,12</sup>

In the first study, a nested case-control study by Johannes et al,<sup>11</sup> domperidone use was associated with an increased risk of serious ventricular arrhythmia (SVA) and SCD when compared with nonusers (adjusted odds ratio [AOR] 1.59, 95% CI 1.28 to 1.98). The average age for the cohort was 79.4 years (range 20 to 95, median age 82); when stratified by age and sex, individuals younger than age 60 years and women did not have increased risk from domperidone exposure (OR [95% CI]

1.10 [0.35 to 3.47] and 1.25 [0.93 to 1.67], respectively).<sup>11</sup>

In the second study, a case-control analysis by van Noord et al,<sup>12</sup> current domperidone use was associated with increased risk of SCD (unadjusted OR 3.72, 95% CI 1.72 to 8.08), but the AOR was not significant. When the authors further focused on publicly insured patients, which included 7 SCD cases with current domperidone use, the AOR became significant (AOR 4.17, 95% CI 1.33 to 13.1). Investigators were unable to demonstrate an effect of domperidone on SVA owing to an absence of exposed cases. When stratified by daily dose, doses above 30 mg/d were associated with higher risk of SCD (AOR 11.4, 95% CI 1.99 to 65.2). This association, however, was based on only 4 individuals exposed to domperidone who experienced SCD. Also of importance, the average (SD) age of the cohort of SCD cases (n=1304) was 72.5 (14.1) years. Clearly, the populations in these studies are distinct from healthy breastfeeding women.<sup>12</sup>

Finally, in both studies, the data on the cases and controls were retrieved from databases. These databases have some limitations. One of the main limitations is that the researchers were only able to examine if a prescription for domperidone was filled. Whether or not the individual took the medication was not confirmed.<sup>11,12</sup> Also, in the Netherlands, where the second study was conducted, domperidone is available over the counter; therefore, all exposures to domperidone might not have been captured.<sup>12</sup>

## Conclusion

Owing to the demographic characteristics of the populations in both studies,<sup>11,12</sup> the risks reported in these papers would not directly apply to healthy women of childbearing age. Nonetheless, caution is advised when prescribing domperidone with other drugs that prolong the QT interval or with those that interfere with domperidone metabolism, or for women who have underlying cardiac diseases.<sup>1</sup>

### Competing interests

None declared

### References

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Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7562; they will be addressed in future Motherisk Updates.

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