



## **Summary Safety Review - Gentian violet-containing human health products - Assessing the potential risk of cancer**

**Product:** Gentiane Violet Liquid Topical (gentian violet) and Hydrofera Antibacterial Foam Dressings

**Potential Safety Issue:** Cancer

### **Key Messages**

- **Gentiane Violet Liquid Topical (gentian violet) is a non-prescription drug that has been used to treat infections of the skin (cutaneous) and inside the nose, mouth, and vagina (mucocutaneous). Gentian violet can also be found in Hydrofera Antibacterial Foam Dressings, which are used as external dressings for wounds.**
- **Health Canada conducted two health risk assessments on gentian violet-containing human therapeutic products: one on the non-prescription drug product and one on the medical devices (foam dressings). These assessments were triggered by the World Health Organization's Codex Alimentarius Commission recommending that regulatory authorities prevent exposure to gentian violet in food because of its potential to cause cancer.<sup>1</sup>**
- **Health Canada's risk assessment of the non-prescription drug product concluded that there is evidence based on animal studies in the scientific literature of a potential for a link between gentian violet and cancer. In studies, cases of cancer in animals following oral exposure of gentian violet were noted. There have been no reported cases of cancer in humans associated with the use of topical gentian violet in Canada or internationally.**
- **Health Canada notified the manufacturer of Gentiane Violet Liquid Topical of the results of the assessment. The manufacturer agreed to voluntarily discontinue marketing of their product in Canada and their health product drug licence has been cancelled.**
- **Health Canada's risk assessment of medical devices containing gentian violet concluded, based on the limited exposure to gentian violet, that the risk of cancer is unlikely. However, no clinical data to support the safety and effectiveness of the device for pregnant and nursing women has been provided, and as a precaution, Health Canada will work with the manufacturers to update the Instructions for Use to strengthen existing warnings.**
- **An Information Update will be published to give Canadians more details about this risk, what consumers should do, and further actions taken by Health Canada.**
- **Following a separate risk assessment for veterinary drugs, manufacturers of these products also agreed to voluntarily discontinue marketing their products in Canada and their drug licence has been cancelled.**

## Overview

Gentian violet has been used in health products for both humans and animals. In humans, gentian violet has been used to treat infections of the skin, and as an antibacterial dye in external foam wound dressings.

In 2014, the [FAO/WHO Joint Expert Committee on Food Additives \(JECFA\)](#) completed an assessment (toxicological evaluation) of certain veterinary drugs (including gentian violet) residues in food. They concluded that gentian violet can alter genetic material and cause cancer (genotoxic carcinogen). Therefore, an acceptable daily intake (ADI) cannot be established. Based on the JECFA's conclusion, the Codex Alimentarius Commission, which develops international food standards to protect consumer health and to facilitate fair trading practices in foods, recommended in 2018 that regulatory authorities prevent exposure to residues of gentian violet in food.<sup>1</sup> Following this recommendation, Health Canada decided to review the risk of cancer with the use of gentian violet-containing human health products, in addition to veterinary products.

## Use in Canada

- Gentiane Violet Liquid Topical has been marketed in Canada since 1951. The first licence for a Hydrofera Antibacterial Foam Dressing was issued in 2012.
- Gentiane Violet Liquid Topical is a non-prescription drug product used to treat infections of the skin (cutaneous), including the nose, mouth, and vagina (mucocutaneous). As a result of Health Canada's risk assessment, the manufacturer of the product informed Health Canada in May 2019 that they will voluntarily stop marketing this product in Canada and their health product licence has been cancelled.
- Hydrofera Antibacterial Foam Dressings are medical devices used as external dressings for wounds such as sores (e.g., pressure ulcers, venous stasis ulcers, arterial ulcers, diabetic ulcers), skin graft donor sites, abrasions and cuts (lacerations), superficial burns, post-surgical incisions, and other external wounds.
- In animals, gentian violet has been used topically for the treatment of surface wounds and eye infections.

## Safety Review Findings

- Health Canada received 4 Canadian reports<sup>a</sup> of adverse events associated with the use of gentian violet-containing drug products. The reported adverse events include localized skin reactions, pain, discomfort, and local discoloration. Of these 4 reports, 2 involve infants (2 months and 5 months of age). These reports confirm the use of gentian violet to treat oral thrush in infants.

- Health Canada also identified 50 international reports involving the use of a gentian violet-containing drug product from VigiBase<sup>b</sup>, 4 of which were considered serious.
- While there have been no Canadian nor international reports of cancer associated with the human use of gentian violet, animal studies show a link between gentian violet and cancer when ingested. It is unknown if applying gentian violet to the skin (topical application) has the same cancer causing effect.
- Some evidence suggests health products containing gentian violet are being used in infants and breastfeeding mothers. As such, it is possible that when gentian violet is applied to the nipple of the breast and/or used to treat thrush, it may be ingested by infants.
- Health Canada also reviewed the risk of cancer with the use of Hydrofera Antibacterial Foam Dressings. The gentian violet in these medical devices is not intended to be released, absorbed or ingested under normal conditions of use. Evidence shows that because of the structure and composition of the medical devices, little to no gentian violet is exposed to the human body. Although the exposure to gentian violet from these medical devices is limited, no clinical data to support the safety and effectiveness of the device for pregnant and nursing women was provided to Health Canada by the manufacturer. As a precaution, Health Canada will work with the manufacturer to strengthen the device safety information to better inform users.

### **Conclusions and Actions**

- Health Canada conducted two health risk assessments on gentian violet-containing products: one focused on a non-prescription drug product and the other on medical devices (foam dressings).
- Health Canada's risk assessment of the non-prescription drug product concluded that there is evidence in the scientific literature, based on animal studies, that there is a potential for gentian violet to cause cancer. Although no cases of cancer associated with the use of topical gentian violet were found, oral exposure of gentian violet has been shown in animal studies to cause cancer.
- Health Canada contacted the manufacturer and notified them of the results of the assessment noting the potential risk of cancer with the use of gentian violet-containing drug products. The manufacturer of Gentiane Violet Liquid Topical voluntarily discontinued the sale of the product in Canada in May 2019, and their health product drug licence has been cancelled.
- Consumers are advised to stop using Gentiane Violet Liquid Topical and return it to their local pharmacy for proper disposal.
- Health Canada's assessment of gentian violet-containing medical devices found that because of the structure and composition of the medical devices, little to no gentian violet

is exposed to the human body. However, no clinical data to support the safety and effectiveness of the device for pregnant and nursing women was provided to Health Canada by the manufacturer.

- As a precaution, Health Canada will work with the manufacturer to strengthen the device safety information to better inform users.
- Additionally, any new medical device licence applications listing gentian violet as a component will be reviewed to determine maximum exposure risks.
- Health Canada has also looked at veterinary drugs that contain gentian violet and manufacturers of the 9 impacted veterinary drug products have agreed to voluntarily discontinue marketing their products in Canada and their drug licence have been cancelled.
- An Information Update will be published to give Canadians more details about this risk, what consumers should do, and further actions taken by Health Canada.

### **Additional Information**

The analysis that contributed to this risk assessment included scientific and medical literature, Canadian and international adverse reaction reports, and what is known about the use of these drugs and medical devices both in Canada and internationally.

For additional information, contact the Marketed Health Products Directorate.

If manufacturers of medical devices or industry associations require more information at this time, they are encouraged to contact the Therapeutic Products Directorate ([hc.tpdgeneral-generalcpt.sc@canada.ca](mailto:hc.tpdgeneral-generalcpt.sc@canada.ca)).

### **Reference**

1. [Codex Alimentarius Commission: 02-06 July 2018](#)

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- a. Canadian reports can be accessed through the [Canada Vigilance Online Database](#)
  - b. VigiBase is the WHO global database of individual case safety reports. This information comes from a variety of sources, and the likelihood that the suspected adverse reaction is drug-related is not the same in all cases. This information does not represent the opinion of the World Health Organization.