

Summary Safety Review - Sofosbuvir-containing products - Assessing the Potential Risk of Severe Cutaneous Adverse Reactions

Product: Sofosbuvir-containing products

Potential Safety Issue: Severe cutaneous adverse reactions (SCAR), a group of serious, potentially life-threatening, adverse reactions to drugs that involve the skin and inner lining of some organs.

Key Messages

- **Sofosbuvir-containing products are authorized for sale in Canada to treat chronic hepatitis C virus infection.**
- **Health Canada reviewed the potential risk of severe cutaneous adverse reactions (SCAR) with the use of sofosbuvir-containing products. This safety review was triggered by updates made by the European Medicines Agency (EMA) to the product safety information for sofosbuvir-containing products to include the risk of Stevens - Johnson syndrome (SJS), a type of SCAR. The purpose of this review was to determine if similar actions were required in Canada.**
- **Health Canada's review of the available information concluded that there may be a link between the use of sofosbuvir-containing products and the risk of Stevens - Johnson syndrome, but did not confirm a link with other types of SCAR.**
- **Health Canada will be working with the manufacturer to update the Canadian product safety information for sofosbuvir-containing products to inform healthcare professionals and patients about the risk of SJS.**

Overview

Health Canada reviewed the potential risk of severe cutaneous adverse reactions (SCAR) in patients treated with sofosbuvir-containing products. The safety review was initiated when Health Canada became aware that the EMA updated the product safety information for all sofosbuvir-containing products with new information on the risk of Stevens - Johnson syndrome (SJS). The purpose of this review was to determine whether similar actions were required in Canada.

SCAR is a group of serious, potentially life-threatening, adverse reactions to drugs that involve the skin and inner lining of some organs. This safety review focused on specific types of SCAR: SJS and Toxic Epidermal Necrolysis (TEN) (a more severe form of SJS), Acute Generalized Exanthematous Pustulosis (AGEP), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), Erythema Multiforme (EM) and Bullous Dermatitis (BD). While rare, SCAR can lead to hospitalization and death in some cases.

Use in Canada

- Sofosbuvir-containing products are prescription drugs authorized for sale in Canada to treat chronic hepatitis-C virus infection.
- Sofosbuvir has been marketed in Canada as a single-ingredient product since 2014 (Sovaldi), and as a combination product with other ingredients since 2014 (Harvoni), 2016 (Eplusa), and 2017 (Vosevi).
- Sovaldi is available in 400 mg sofosbuvir tablets. Harvoni comes in tablets of 90 mg/400 mg ledipasvir/sofosbuvir. Eplusa is available in tablets of 400 mg/100 mg sofosbuvir/velpatasvir. And, Vosevi comes in tablets of 400 mg/100mg/100 mg sofosbuvir/velpatasvir/voxilaprevir.
- There were about 100,000 prescriptions filled annually in Canada for these products between 2015 and 2019.

Safety Review Findings

- Health Canada reviewed the available information from searches of the Canada Vigilance database^a, international databases, published literature and information provided by the manufacturer.
- Health Canada reviewed 13 case reports (all foreign) of SCAR in patients receiving sofosbuvir-containing products. Of the 13 case reports, 6 reports involved SJS/TEN (4 SJS, 1 TEN and 1 unclear whether SJS or TEN), 5 reports involved EM, and 2 involved BD.
 - Of the 6 SJS/TEN case reports, 1 case (SJS) was found to be probably linked to the use of sofosbuvir-containing products, 4 cases were possibly linked (2 SJS, 1 TEN, 1 TEN/SJS), and 1 case (SJS) was unlikely to be linked.
 - Of the 5 EM case reports, 4 cases were found to be possibly linked to the use of sofosbuvir-containing products, and one report could not be assessed further due to limited information in the report, co-existing medical conditions, and other drugs the patient was taking at the same time. Assessing the risk of erythema multiforme in these reports was challenging because hepatitis C is a possible cause of EM.
 - The two cases of BD could not be assessed further due to several contributing factors such as incomplete information about pre-existing medical conditions, lack of detailed information in the reports, and co-existing infections that may have contributed to BD.

Conclusions and Actions

- Health Canada's review of the available information concluded that there may be a link between the use of sofosbuvir-containing products and the risk of SJS, but did not confirm a link with the risk of other types of SCAR.
- Health Canada will work with the manufacturer to update the Canadian product safety information for all sofosbuvir-containing products to include the risk of SJS in the Post-Market Adverse Drug Reactions section.
- Health Canada will continue to monitor safety information involving sofosbuvir-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 sofosbuvir-containing products both in Canada and internationally.

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

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