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(來函請敘明此檔案號碼) DH DO DIMC/7-30/1  
(IN REPLY PLEASE QUOTE THIS FILE REF.)

29 May 2026

Dear Healthcare Professionals,

### **Diosmin and Hesperidin: Assessing the Potential Increased Risk of Bleeding**

Your attention is drawn to the following Health Canada's announcement.

#### **Product**

- Diosmin-containing natural health products (NHPs)
- Diosmin- and hesperidin-containing NHPs

#### **Potential Safety Issue**

Increased risk of bleeding

#### **Key Messages**

- Health Canada's review of the available information found a possible link between the use of either diosmin or diosmin in combination with hesperidin, and the increased risk of bleeding.
- Although there is a possible increased risk of bleeding with the use of either diosmin or diosmin in combination with hesperidin across the general population, evidence suggests that the severity of bleeding may be greater in individuals who are taking medications that affect blood clotting, such as anticoagulants (also known as blood thinners).
- Health Canada will update the related monographs to include a recommendation for consumers to consult a healthcare professional prior to taking the product if they are taking medications, including anticoagulants.
- Health Canada expects licence holders to update the risk information on product labels for all licensed diosmin-containing NHPs, as well as diosmin- and hesperidin-containing NHPs, to include a recommendation for consumers to consult a healthcare professional prior to taking the product if they are taking medications, including anticoagulants.
- Health Canada will also inform healthcare professionals about these updates through a Health Product InfoWatch communication.

## **Overview**

Health Canada reviewed the potential increased risk of bleeding with the use of either diosmin or diosmin in combination with hesperidin. This safety review was triggered by a Canadian case of severe rectal bleeding in a patient who had been taking Hemovel, a diosmin-containing NHP, in combination with other medications (including an anticoagulant), for 2 days.

Bioflavonoids are a diverse group of phytochemicals (compounds produced by plants to provide colour, flavour and protection against pests or disease). Diosmin and hesperidin are bioflavonoids present in a number of plants, including citrus fruits (also known as citrus bioflavonoids). As medicinal ingredients, diosmin and hesperidin may be present in a variety of NHPs, including those for the relief of symptoms of hemorrhoids, varicose veins and chronic venous insufficiency. In addition to diosmin and hesperidin, there are many compounds that are classified as citrus bioflavonoids. However, this safety review only focused on diosmin and hesperidin as Health Canada had not received reports of bleeding events concerning other citrus bioflavonoids.

## **Use in Canada**

- Diosmin and hesperidin are authorized in Canada for use in NHPs for their antioxidant effects (helps protect cells from harmful free radicals, which have been linked to certain health conditions), and for the relief of symptoms of venous insufficiency (failure of veins to adequately circulate blood), varicose veins (swollen veins that bulge under the surface of the skin) and hemorrhoids (swollen veins in the anus and lower rectum).
- Health Canada has authorized diosmin- and/or hesperidin-containing NHPs (either as a single ingredient product or in combination with other ingredients) for oral use under the Natural Health Products Regulations.
- In Canada, diosmin-containing NHPs, with or without hesperidin, are the primary available treatments to help strengthen vein walls and improve circulation in people with chronic venous insufficiency.

## **Safety Review Findings**

- Health Canada reviewed the available information from searches of the Canada Vigilance database, the World Health Organization's (WHO) adverse drug reaction database and the scientific literature.
- Health Canada reviewed 19 cases (4 Canadian and 15 international) of bleeding events in patients taking either diosmin or diosmin in combination with hesperidin, including 1 case from the published literature. Of the 19 cases, 4 international cases were found to be possibly linked to the use of either diosmin or diosmin in combination with hesperidin, and the remaining 15 (4 Canadian and 11 international) were unassessable due to limited clinical information and the presence of confounders (other factors that may have contributed to the occurrence of bleeding), such as underlying medical conditions, and the use of prescription drugs and other NHPs. Two deaths (1 Canadian and 1 international) were reported among the unassessable cases.

- Health Canada also reviewed the scientific literature and real-world evidence, which suggested the presence of multiple factors that could increase the risk of bleeding when using either diosmin or diosmin in combination with hesperidin.
  - o The scientific literature provided evidence that diosmin may interfere with how certain medications, including anticoagulants, function in the body, such as how they are cleared and/or eliminated from the body. This could result in increased levels of anticoagulants in the blood, increasing their blood thinning effects and the risk of bleeding. Some manufacturers of diosmin-containing health products and diosmin- and hesperidin-containing health products marketed in other countries, such as the United States and Australia, have voluntarily updated the risk information on the product labels for these products to include warnings about their use with anticoagulants or during medical procedures.
  - o Studies have also shown that diosmin and hesperidin can themselves have blood-thinning effects.

### **Conclusions and Actions**

- Health Canada's review found a possible link between the use of either diosmin or diosmin in combination with hesperidin and the increased risk of bleeding.
- Although there is a possible increased risk of bleeding with the use of either diosmin or diosmin in combination with hesperidin across the general population, evidence suggests that the severity of bleeding may be greater in individuals who are taking medications that affect blood clotting, such as anticoagulants. Health Canada will update the related monographs to include a recommendation for consumers to consult a healthcare professional prior to taking the product if they are taking medications, including anticoagulants.
- Health Canada expects licence holders to update the risk information on product labels for all licensed diosmin-containing NHPs, as well as diosmin- and hesperidin-containing NHPs to include a recommendation for consumers to consult a healthcare professional prior to taking the product if they are taking medications, including anticoagulants.
- Health Canada will also inform healthcare professionals about these updates through a Health Product InfoWatch communication.
- Health Canada will continue to monitor safety information involving diosmin and hesperidin, 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 new health risks be identified.

Please refer to the following website in Health Canada for details:

<https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SSR1775582460008>

In Hong Kong, there are 18 registered pharmaceutical products containing diosmin, of which 17 are combination products with hesperidin. All products are over-the-counter medicines. So far, the Department of Health (DH) has not received any case of adverse drug reaction report with regard to

diosmin or hesperidin. In light of the above Health Canada's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board of Hong Kong.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Clinical Trials and Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: [adr@dh.gov.hk](mailto:adr@dh.gov.hk)). For details, please refer to the website at Drug Office under "ADR Reporting": <http://www.drugoffice.gov.hk/adr.html>. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,



(Clive CHAN)

for Assistant Director (Drug)