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

19 Dec 2025

Dear Healthcare Professionals,

Brukinsa (zanubrutinib), Calquence (acalabrutinib) and Imbruvica (ibrutinib) - Bruton's Tyrosine Kinase (BTK) Inhibitors: Assessing the potential risk of serious hepatotoxicity

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

Product

Brukinsa (zanubrutinib), Calquence (acalabrutinib) and Imbruvica (ibrutinib) - Bruton's tyrosine kinase (BTK) inhibitors

Potential Safety Issue

Serious hepatotoxicity (liver injury), including drug-induced liver injury (DILI; a rare, but potentially life-threatening, drug reaction with elevated liver enzymes that may lead to liver failure or a need for liver transplant)

Key Messages

- Health Canada's review found a possible link between the use of BTK inhibitors and the risk of serious hepatotoxicity.
- Health Canada is working with the manufacturers to update the product safety information in the Canadian product monograph (CPM) for all BTK inhibitors to include the risk of serious hepatotoxicity. Health Canada will also inform healthcare professionals about this update through a Health Product InfoWatch communication.

Overview

Health Canada reviewed the potential risk of serious hepatotoxicity with the use of BTK inhibitors. This safety review was triggered by notifications of foreign action received from manufacturers.

Prior to Health Canada beginning its review, the manufacturer of Imbruvica initiated a labelling update to include the risk of serious hepatotoxicity in the CPM. Health Canada's safety review, therefore,

aimed to determine whether this risk is associated with all other BTK inhibitors (a class effect) and whether a labelling update is warranted across the drug class.

Use in Canada

- Bruton's tyrosine kinase inhibitors are a class of prescription drugs authorized for sale in Canada for the treatment of various blood cancers. In addition, Imbruvica specifically can be used for the treatment of chronic graft-versus-host-disease (a complication of bone marrow transplantation), when other treatments did not work and additional therapy is needed.
- Bruton's tyrosine kinase inhibitors have been marketed in Canada since 2014. All BTK inhibitors are available as oral formulations.
- Approximately 65,000 prescriptions for BTK inhibitors were dispensed by Canadian retail pharmacies in 2024.

Safety Review Findings

- Health Canada reviewed the available information provided by manufacturers and a foreign regulatory agency, as well as from searches of the Canada Vigilance database and the scientific literature.
- Health Canada reviewed 11 cases (1 Canadian and 10 international) of serious hepatotoxicity in patients using Brukinsa or Calquence, including 2 from the published literature. All 11 cases were found to be possibly linked to the use of BTK inhibitors.
- Health Canada also reviewed 20 articles published in the scientific literature. Despite limitations, including the presence of confounders (other factors that may have contributed to the occurrence of hepatotoxicity) and insufficient clinical information, the evidence reviewed supported a possible link between all BTK inhibitors and the risk of serious hepatotoxicity.

Conclusions and Actions

- Health Canada's review of the available information found a possible link between the use of BTK inhibitors and the risk of serious hepatotoxicity.
- Health Canada is working with the manufacturers of BTK inhibitors to update the CPM to include the risk of serious hepatotoxicity. The CPM for Jaypirca (pirtobrutinib), a BTK inhibitor that was authorized for sale in Canada after the completion of this review, will also include this risk.
- Health Canada will also inform healthcare professionals about this update through a Health Product InfoWatch communication.
- Health Canada will continue to monitor safety information involving BTK inhibitors, 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.

Please refer to the following website in Health Canada for details:
https://dhpp.hpfb-dgpsa.ca/review-documents/resource/SSR1762956369249

In Hong Kong, there are registered pharmaceutical products containing zanubrutinib (1 product), acalabrutinib (2 products), ibrutinib (3 products) and pirtobrutinib (2 products). All products are prescription-only medicines. So far, the Department of Health (DH) has received adverse drug reaction reports with regard to acalabrutinib (1 case) and ibrutinib (37 cases), but all these cases were not related to hepatotoxicity, while no adverse drug reaction report with regard to zanubrutinib and pirtobrutinib had been received. Related news on the risk of hepatotoxicity associated with Imbruvica (ibrutinib) was previously issued by Singapore Health Sciences Authority and was posted on Drug Office website on 2 Oct 2024. 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). 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,

P.P.

(Clive CHAN)
for Assistant Director (Drug)