Drug News
藥 物 情 報

Issue Number 186

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in April 2025 with relevant information update before publish. For the latest news and information, please refer to public announcements or the website of the Drug Office of the Department of Health (http://www.drugoffice.gov.hk).

Safety Update

Australia: New safety warnings for isotretinoin (Roaccutane)

On 7 April 2025, the Therapeutic Goods Administration (TGA) announced that additional safety information will be added to all isotretinoin products, further highlighting the recognized potential risks of mood-related changes and sexual disorders. The update includes:

- new advice to conduct a mental health assessment for all patients before starting isotretinoin
- what to do if mood-related changes develop
- new warnings and advice added regarding sexual health-related side effects.

This safety update follows a TGA safety investigation conducted in 2024 after international regulators strengthened warning about psychiatric and sexual disorders for isotretinoin. As a result, the Product Information (PI) and Consumer Medicine Information (CMI) are being updated as a precautionary measure and to align with international regulatory advice.

Isotretinoin, originally sold as Roaccutane, is a prescription medicine used to treat patients with severe cystic acne who have not seen improvement after conventional therapy, including systemic antibiotics.

According to the Australasian College of Dermatologists, patients with acne may suffer from poor body image, low self-esteem, experience social isolation and avoid participating in daily activities, which persist long after the active lesions have disappeared. Increased levels of anxiety, anger, depression, and frustration are also observed among patients with acne, often a result of the emotional impact. The college advises that isotretinoin is effective in treating mild-moderate, severe, persistent and/or scarring acne. The college updated its position statement on the use of isotretinoin for the treatment of acne in October 2024.

The TGA initially investigated the association between isotretinoin and psychiatric adverse reactions in 2016, concluding that the then-current warnings in the Australian PI were appropriate. It published an Medicines Safety Update to remind prescribers of the risks and the need for careful psychological assessment prior to and during isotretinoin treatment. The UK Commission on Human Medicines Isotretinoin Expert Working Group published a report on isotretinoin and the risk of psychiatric and sexual disorders in April 2023. Health Canada published a summary safety review in June 2024 regarding isotretinoin and the potential risk of sexual dysfunction, including persistent sexual dysfunction after drug discontinuation.

The TGA undertook an investigation to review all current information on these safety signals. The investigation concluded that an association between isotretinoin and psychiatric/sexual disorders could not be ruled out. Given the reported cases of severe and sometimes persisting adverse events and that isotretinoin is commonly used to treat severe cystic acne in adolescent populations, it was recommended the PI be updated as a precautionary measure and to align with international regulators.

Changes to the isotretinoin PI include update of relevant text regarding psychiatric disorders and sexual disorders. For details, please refer to the website in TGA.

Health professionals should be alert to the potential psychiatric and sexual disorders associated with isotretinoin. These side effects can result in serious consequences, especially considering that

isotretinoin is often used in adolescents. Health professionals should be alert to patients who show signs of: depression; psychotic behaviours; suicidal thoughts and actions (rare); sexual dysfunction, including erectile dysfunction; decreased sex drive (libido); vulvovaginal dryness; feeling numb or indifferent (anhedonia); and enlarged breasts in males (gynaecomastia).

Before initiating isotretinoin, prescribers are advised to assess patients' mental health as well as their family history of mental health conditions. Health professionals should monitor for depression and sexual disorders both before and during treatment. If these symptoms occur, cease treatment immediately. It is possible that discontinuation of treatment may not alleviate symptoms and further specialist evaluation may be necessary.

In Hong Kong, there are 13 registered pharmaceutical products containing isotretinoin. All products are prescription-only medicines. As of the end of April 2025, with regard to isotretinoin, the Department of Health (DH) had received 2 cases of adverse drug reaction, but these cases were not related to psychiatric and sexual disorders.

Related news was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 96, with the latest update reported in the Drug News Issue No. 177. The DH issued letters to inform local healthcare professionals to draw their attention on 27 October 2017 and 27 April 2023. In October 2024, the Registration Committee of the Pharmacy and Poisons Board discussed the matter and decided that the sales pack labels and/or package inserts of locally registered pharmaceutical products containing isotretinoin should contain the strengthened safety information about the risk of psychiatric and sexual disorders. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

The United Kingdom: Short-acting beta 2 agonists (SABA) (salbutamol and terbutaline): reminder of the risks from overuse in asthma and to be aware of changes in the SABA prescribing guidelines

On 24 April 2025, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that healthcare professionals and patients are reminded of the risk of severe asthma attacks and increased mortality associated with overuse of SABA with or without anti-inflammatory maintenance therapy in patients with asthma. Healthcare professionals should be aware of the change in guidance that no longer recommends prescribing SABA without an inhaled corticosteroid.

The asthma reliever medications salbutamol and terbutaline are prescription-only SABA medications used to treat breathing problems in people with asthma and similar conditions. Prior to December 2024, inhaled SABA was recommended to be used as required as reliever therapy for people with symptomatic asthma. In a small minority of people with asthma with infrequent, short-lived wheeze, and normal lung function, occasional use of inhaled SABA reliever therapy was considered as potentially the only treatment needed to manage their symptoms.

A review of the risk of SABA overuse was initiated in the UK by the MHRA and in the EU by the Pharmacovigilance Risk Assessment Committee (PRAC) in 2022. The evidence reviewed included published observational data from 187,675 UK primary care electronic health care records from patients with asthma aged 12 years and over as well as similar data from other participating countries. An association was identified in the UK across all asthma severities between having 3 or more SABA prescriptions over the 1-year study period and experiencing severe asthma exacerbations. This association was independent of the use of anti-inflammatory maintenance asthma therapy.

Based on the findings of the review, regulatory action was taken in 2023 to strengthen the warnings in the approved UK product information for SABA medications on the risk of masking asthma deterioration by overuse of SABA relievers. Advice was also included on the importance of regular use of preventer medication even when asthma is well controlled and when a reliever inhaler is rarely needed; recommending that patients seek medical attention as soon as possible if their use of a SABA reliever inhaler increases. This is to ensure timely re-evaluation of asthma treatment.

The UK asthma guidelines were updated in November 2024 following a review of the evidence from multiple sources including national reviews of asthma deaths in both adults and children. The evidence highlighted that clinical outcomes with asthma were poorest in all age groups when using

SABA alone. SABA overuse was associated with an increased risk of severe asthma exacerbations, hospitalisations and mortality irrespective of asthma severity or co-administration of anti-inflammatory therapy. As a result, in accordance with the updated UK asthma guidelines, the prescribing of inhaled SABA monotherapy for people of any age with asthma without prescribing a concomitant approved asthma preventer anti-inflammatory medication is no longer recommended. The guidance now recommends that the majority of people with asthma should be controlled on either anti-inflammatory reliever (AIR) or maintenance and reliever therapy (MART) treatment without the need for SABA. The personalised asthma action plan should be reviewed at every asthma review to ensure pharmacological treatment is optimised if asthma control is suboptimal.

A report was published in December 2024 by the UK National Child Mortality Database Programme on child deaths which occurred between April 2019 and March 2023 due to asthma or anaphylaxis. The findings confirmed previous evidence on the risks associated with overuse of SABA. Of the 54 child deaths due to asthma which were identified, 87% (47) had an excessive number of reliever inhalers (three or more) dispensed in the year before their death, with 27 children (50%) having 12 or more reliever inhalers dispensed. Furthermore, for 35 (65%) children, there was insufficient dispensing of preventer inhalers with fewer than 9 dispensed in the year preceding their death, and 23 (43%) children receiving 4 or fewer preventer inhalers.

Advice for Healthcare Professionals:

- Excessive use of SABA to relieve acute asthma symptoms may mask progression of the underlying disease and contribute to an increased risk of severe and potentially life-threatening asthma exacerbations.
- Do not prescribe SABA to people of any age with asthma without a concomitant prescription of an inhaled corticosteroid (see Asthma: diagnosis, monitoring and chronic asthma management (BTS, NICE, SIGN) NICE guideline [NG245], 2024).
- Ensure all patients with asthma receive optimal anti-inflammatory maintenance therapy even when their asthma is well controlled and that treatment is individualised to the patient.
- Review and adjust asthma treatment in patients who take more than twice weekly "as needed" SABA.
- Urgently review patients where there has either been an increase in the number of prescriptions requested for SABA reliever inhalers or a failure to collect prescribed anti-inflammatory maintenance treatment.
- AIR therapy and MART are recommended alternatives for people over 12 years of age with poorly controlled asthma.

In Hong Kong, there are 45 registered pharmaceutical products containing salbutamol, of which 13 products are for inhalation. There are 20 registered pharmaceutical products containing terbutaline, of which none are for inhalation. As of the end of April 2025, the Department of Health (DH) had received 8 cases of adverse drug reaction with regard to salbutamol, but these cases were not related to severe asthma exacerbation or death. The DH had not received any case of adverse drug reaction with regard to terbutaline.

The risk of asthma exacerbation and increased mortality related to overuse of salbutamol and terbutaline inhaler is documented in overseas reputable drug references such as "Martindale: The Complete Drug Reference". The DH will remain vigilant on safety update of the drugs issued by other overseas drug regulatory authorities.

Canada: Summary Safety Review: Cyclin-dependent kinase inhibitors (abemaciclib, palbociclib and ribociclib) and HMG-CoA reductase inhibitors (atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin and simvastatin) (Statins): Assessing the potential risk of rhabdomyolysis due to drug interaction

On 24 April 2025, Health Canada announced that it reviewed the potential risk of rhabdomyolysis and the drug interaction between cyclin-dependent kinase inhibitors (CDKIs) and HMG-CoA reductase inhibitors, more commonly known as statins. The safety review was triggered by the European Medicines Agency (EMA)'s investigation of the risk with palbociclib and statins.

Rhabdomyolysis is a rare and potentially life-threatening condition in which muscles break down and their contents are released into the blood stream. This can lead to organ damage, such as kidney failure. Rhabdomyolysis is a known risk associated with statins. Some drugs may increase

the body's exposure to statins, thereby increasing the patient's risk of statin-related rhabdomyolysis. Though the risk of rhabdomyolysis is known and well labelled for statins, this review investigated the potential risk of rhabdomyolysis due to the drug interaction between CDKIs and statins.

Cyclin-dependent kinase inhibitors are a class of prescription drugs authorized for sale in Canada for the treatment of a specific, but common, type of breast cancer. Statins are prescription drugs authorized for sale in Canada, to be used along with diet, to lower cholesterol and triglyceride (fat) levels in the blood, and to reduce the risk of heart attack or stroke in patients with risk factors for heart problems.

Health Canada reviewed the available information provided by the manufacturers, as well as from searches of the Canada Vigilance database and the scientific literature. Health Canada reviewed 13 cases (1 Canadian and 12 international) of rhabdomyolysis in patients taking both a CDKI (palbociclib or ribociclib) and statin (rosuvastatin or simvastatin). All 13 cases were found to be possibly linked to the drug interaction between CDKIs and statins. There were no deaths reported among the cases. In all 13 cases, patients had been on statin therapy prior to starting CDKI therapy. In 8 of those cases, statin therapy was ongoing without reported rhabdomyolysis for over 1 year prior to the start of CDKI therapy. In 6 of these 8 cases, rhabdomyolysis occurred within 30 days of the addition of a CDKI, which suggests the possibility that CDKI introduction increased the body's exposure to statins, leading to rhabdomyolysis.

While a drug interaction between CDKIs and statins is not currently labelled for either class of product, information contained in the Canadian product monograph (CPM) concerning how they work in the body supports the possibility of a drug interaction. Health Canada also reviewed a study that investigated the potential interaction between palbociclib and atorvastatin using computer simulation. This study suggested that 125 mg/day of palbociclib could moderately increase the exposure of 40 mg/day atorvastatin in healthy volunteers, thereby potentially increasing the risk of rhabdomyolysis.

Although observed rhabdomyolysis cases were limited to the combined administration of palbociclib or ribociclib, and rosuvastatin or simvastatin, the totality of evidence supports the precautionary conclusion that rhabdomyolysis is a potential risk due to a drug interaction between CDKIs and statins.

Health Canada's review of the available information found a possible link between rhabdomyolysis and the drug interaction between CDKIs and statins. Health Canada will work with the manufacturers to update the CPM for all CDKIs to include the risk of rhabdomyolysis due to the drug interaction with statins. Health Canada will also inform healthcare professionals about this update through a Health Product InfoWatch communication.

In Hong Kong, there are registered pharmaceutical products containing abemaciclib (3 products), palbociclib (6 products) and ribociclib (1 product). All products are prescription-only medicines. As of the end of April 2025, the Department of Health (DH) had received adverse drug reaction with regard to abemaciclib (26 cases), palbociclib (147 cases) and ribociclib (28 cases), but these cases were not related to drug interaction.

In light of the above Health Canada's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 25 April 2025, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Batch recall of two products of Pms-Fluoxetine capsules due to presence of impurity

On 29 April 2025, the Department of Health (DH) endorsed a licensed drug wholesaler, Trenton-Boma Limited (Trenton-Boma), to recall a total of eight batches of the following two products from the market as a precautionary measure due to the presence of impurity in the products.

Drug Recall

Name of product	Hong Kong registration number	Batch number
Pms-Fluoxetine Capsules 10mg	HK-61931	643518
		644912
		647317
		648682
		653478
		655449
Pms-Fluoxetine Cap 20mg	HK-59714	641413
		645412

The DH received notification from Trenton-Boma that the overseas manufacturer of the products is recalling the above batches of Pms-Fluoxetine capsules as they exceed the accepted level of an impurity, N-nitroso-fluoxetine. N-nitroso-fluoxetine is classified as a probable human carcinogen based on results from laboratory tests. As a precautionary measure, Trenton-Boma is voluntarily recalling the affected batches of products from the market.

The above products, containing fluoxetine, are prescription medicines used for the treatment of depression. According to Trenton-Boma, the affected batches of products have been imported into Hong Kong and supplied to the private doctors, veterinary surgeon, private hospitals and pharmacies, and re-exported to Macao.

As of the end of April 2025, the DH had not received any adverse reaction reports in connection with the products. A notice was posted in the Drug Office website on 29 April 2025 to alert the public of the product recall. The DH will closely monitor the recall.

A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. Part 1 poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part 1 poisons and unregistered pharmaceutical products are offences under the Pharmacy and Poisons Ordinance (Cap. 138). The maximum penalty is a fine of $100,000 and two years' imprisonment for each offence. Antibiotics can only be supplied at registered pharmacies by registered pharmacists or under their supervision and upon a doctor's prescription. They should only be used under the advice of a doctor. Illegal sale or possession of antibiotics are offences under the Antibiotics Ordinance (Cap. 137) and the maximum penalty is a $50,000 fine and one year's imprisonment for each offence.

Under the Import and Export Ordinance (Cap. 60), pharmaceutical products must be imported or exported under and in accordance with an import or export licence issued under the Import and Export Ordinance. Illegal import or export of pharmaceutical products are offences under the Import and Export Ordinance (Cap. 60) and the maximum penalty is a fine of $500,000 and 2 years' imprisonment.

Update on Drug Office's website: You can now search the newly registered medicines in the past year at http://www.drugoffice.gov.hk/eps/drug/newsNRM60/en/healthcare_providers?pageNoRequested=1.
Details of ALL registered pharmaceutical products can still be found in the Drug Office website at http://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/news_informations/reListRPP_index.html.

Useful Contact

Drug Complaint:

Tel: 2572 2068
Fax: 3904 1224
E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920
Fax: 2319 6319
E-mail: adr@dh.gov.hk
Link: http://www.drugoffice.gov.hk/adr.html
Post: Clinical Trials and Pharmacovigilance Unit,
Drug Office, Department of Health,
Suite 2002-05, 20/F, AIA Kowloon Tower, Landmark East,
100 How Ming Street,
Kwun Tong, Kowloon

The purpose of Drug News is to provide healthcare professionals with a summary of local and overseas drug safety news released. Healthcare professionals are advised to keep update with the information and provide corresponding advice or therapeutic measure to patients and public.