Drug News
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This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in March 2021 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

Canada: Summary Safety Review: Cefuroxime-containing products: Assessing the potential risk of Kounis syndrome

On 4 March 2021, Health Canada announced that it reviewed the potential risk of Kounis syndrome with the use of cefuroxime-containing products. The safety review was triggered by foreign case reports published in the medical literature.

Kounis syndrome may occur when an allergic event, including a severe allergic reaction (anaphylactic reaction), results in a sudden reduction of blood flow to the heart. This rare condition may be due in part to a sudden narrowing of the arteries and could lead to the weakening of the heart.

Health Canada reviewed the available information from searches of the Canada Vigilance database, international databases and published literature. Health Canada assessed 10 case reports (all foreign) of Kounis syndrome related to cefuroxime use, including 9 published in the literature. Of the 10 case reports, 8 were found to be possibly linked to the use of cefuroxime while 2 cases did not have enough information to be assessed. No fatalities were reported. Assessing the risk of Kounis syndrome related to the use of cefuroxime-containing products in these reports was challenging due to several contributing factors, including incomplete case details, inconsistent definitions of Kounis syndrome being used, existing medical conditions and other medications taken by the patients. The review of these reports did not support a link between the use of cefuroxime-containing products and the risk of Kounis syndrome. There was insufficient information in these reports to confirm the role of cefuroxime as being the trigger of the severe allergic reactions, and the role of other medications as the cause of Kounis syndrome could not be ruled out.

Health Canada's review of the available information could not confirm a link between the use of cefuroxime-containing products and the risk of Kounis syndrome. Health Canada will continue to monitor safety information involving cefuroxime-containing products, as it does for all health products on the Canadian market.

In Hong Kong, there are 39 registered pharmaceutical products containing cefuroxime. All products are prescription-only medicines. As on 7 April 2021, the Department of Health (DH) has received 4 cases of adverse drug reaction related to cefuroxime, but these cases are not related to Kounis syndrome. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Canada: Pfizer-BioNTech COVID-19 Vaccine: Updated storage and transportation conditions

On 8 March 2021, Health Canada announced that, at the time of authorization, the Pfizer-BioNTech COVID-19 Vaccine Product Monograph (PM) and vial and carton labels indicated that prior to use, the vaccine should only be stored/transported in an ultra -low temperature freezer between -80°C to -60°C. Based on updated information, vials may also be stored/transported at -25°C to -15°C for a period of up to 2 weeks. Vials must be kept frozen and protected from light, in the original cartons, until ready to use. Vials stored/transported at -25°C to -15°C for up to 2 weeks may be returned once to the recommended storage condition of -80°C to -60°C.

In addition, available updated data support transportation of thawed undiluted vials at 2°C to 8°C for up to 12 hours. Thawed undiluted vials

should be stored at 2°C to 8°C for no more than 120 hours (5 days). Any hours used for transport at 2°C to 8°C count against the 120-hour limit for storage at 2°C to 8°C.

Health Canada has authorized updates to the Pfizer-BioNTech COVID-19 Vaccine PM to reflect the new information.

In Hong Kong, the above product is not a registered pharmaceutical product under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). Related news was previously issued by the US Food and Drug Administration (FDA), and was reported in the Drug News Issue No. 136. The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

Australia: COVID-19 vaccines - safety and effectiveness in older adults

On 10 March 2021, the Therapeutic Goods Administration (TGA) announced that extensive vaccine experience has found no safety concerns in older people. The TGA continues to review data from Australia and overseas relating to the safety and effectiveness of COVID-19 vaccines in older adults. The monitoring has not detected any new safety signals in relation to COVID-19 vaccines to date.

The approved Product Information in Australia does not include an upper age limit for the use of either of the two vaccines currently registered in Australia. The decision to vaccinate an older person should be made on a case-by-case basis with consideration of the potential risks and benefits for the individual.

The TGA reviews the safety data from other international medicines regulators of countries with extensive COVID-19 vaccine experience, which have found that no new safety concerns from use of the vaccines in older people:

- The European Medicines Agency (EMA) found no specific safety concern for vaccine use in frail elderly people in its review of worldwide safety data and reports of suspected side effects in Europe for the Pfizer/BioNTech vaccine, Comirnaty. This review included an assessment of reports of death following vaccination in elderly people in Norway.
- The United Kingdom (UK) Medicines and Healthcare products Regulatory Agency (MHRA) found that the overall safety experience with the Pfizer/BioNTech and AstraZeneca COVID-19 vaccines is so far as expected from clinical trials. Review of individual reports and patterns of reporting of cases with a fatal outcome does not suggest that the vaccines played a role in deaths reported in the UK.
- The United States (US) Centers for Disease Control and Prevention found that most reports of adverse events to the US Vaccine Adverse Event Reporting System (VAERS) were of non-serious events. An analysis of deaths in aged care facilities found no unexpected pattern that might suggest a causal relationship with vaccination.

Many people vaccinated so far in Australia have been older, with pre-existing medical conditions. Older age and underlying illnesses make it more likely that coincidental adverse events, including deaths, will occur.

The TGA has received some reports in which an older Australian died after receiving the COVID-19 vaccine. None of these deaths are thought to be caused by vaccination. The TGA is reviewing these reports together with the relevant state and territory health departments. This process includes considering the individual's health status and medical history at the time of vaccination, and where possible involves the individual's health professionals.

The TGA also found promising UK real-world data on vaccine effectiveness in older adults. Two as-yet unpublished studies of vaccine effectiveness in the early months of the vaccine roll-out in England and Scotland indicate the vaccines decrease symptomatic infections and hospitalisations in older people. Results of two studies of the real-world effectiveness of the Pfizer/BioNTech and AstraZeneca COVID-19 vaccines in the United Kingdom have recently been made available. These studies have not yet been peer-reviewed and published in a journal but are available as 'preprints'.

In Hong Kong, the above products are not registered pharmaceutical products under the Pharmacy and Poisons Ordinance (Cap. 138). The

COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). Related news was previously issued by the TGA, and was reported in the Drug News Issue No. 136. The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

European Union: Investigation of COVID-19 Vaccine AstraZeneca and thromboembolic events

On 10 March 2021, the EMA announced that the Austrian national competent authority has suspended the use of a batch of COVID-19 Vaccine AstraZeneca (batch number ABV5300) after a person was diagnosed with multiple thrombosis (formation of blood clots within blood vessels) and died 10 days after vaccination, and another was hospitalised with pulmonary embolism (blockage in arteries in the lungs) after being vaccinated. The latter is now recovering. As of 9 March 2021, two other reports of thromboembolic event cases had been received for this batch.

On 11 March 2021, the EMA announced that it is aware that the Danish Health Authority has paused its vaccination campaign with COVID-19 Vaccine AstraZeneca. This was decided as a precautionary measure while a full investigation is ongoing into reports of blood clots in people who received the vaccine, including one case in Denmark where a person died. Some other Member States have also paused vaccination with this vaccine.

During March 2021, a number of news have been released by various overseas drug authorities, including Health Canada, MHRA, TGA, and EMA reiterating the benefits of the COVID-19 Vaccine AstraZeneca still outweighs its risk.

On 18 March 2021, EMA announced that EMA's safety committee Pharmacovigilance Risk Assessment Committee (PRAC) concluded its preliminary review of a signal of blood clots in people vaccinated with COVID-19 Vaccine AstraZeneca at its extraordinary meeting of 18 Mar 2021. The Committee confirmed that:

- the benefits of the vaccine in combating the still widespread threat of COVID-19 (which itself results in clotting problems and may be fatal) continue to outweigh the risk of side effects;
- the vaccine is not associated with an increase in the overall risk of blood clots (thromboembolic events) in those who receive it;
- there is no evidence of a problem related to specific batches of the vaccine or to particular manufacturing sites;
- however, the vaccine may be associated with very rare cases of blood clots associated with thrombocytopenia, i.e. low levels of blood platelets (elements in the blood that help it to clot) with or without bleeding, including rare cases of clots in the vessels draining blood from the brain (CVST).

The Committee was of the opinion that the vaccine's proven efficacy in preventing hospitalisation and death from COVID-19 outweighs the extremely small likelihood of developing disseminated intravascular coagulation (DIC) or CVST. However, in the light of its findings, patients should be aware of the remote possibility of such syndromes, and if symptoms suggestive of clotting problems occur patients should seek immediate medical attention and inform healthcare professionals of their recent vaccination. Steps are already being taken to update the product information for the vaccine to include more information on these risks. The EMA also provided information for patients and healthcare professionals.

On 25 March 2021, the EMA announced that EMA's safety committee PRAC concluded its preliminary review of cases of blood clots, including very rare cases of blood clots with unusual features such as low numbers of platelets, in people vaccinated with COVID-19 Vaccine AstraZeneca. The committee confirmed that the vaccine is not associated with an increase in the overall risk of blood clots and that the benefits of the vaccine in combating the still widespread threat of COVID-19 continue to outweigh the risk of side effects. The committee recommended including more information and advice for healthcare professionals and the public in the vaccine's product information. The amended product information and the associated direct healthcare professional communication are now available on the EMA website.

PRAC is continuing its assessment of the reported cases. The outcome of the expert meeting, together with further analysis of the reported cases, will feed into PRAC's ongoing evaluation. The PRAC's updated recommendation on the issue is expected

during its April plenary meeting (6–9 April 2021).

In Hong Kong, the above product is not a registered pharmaceutical product.

The United States: The Food and Drug Administration approved revisions to the TRIUMEQ (abacavir ／ dolutegravir ／ lamivudine) and DOVATO (dolutegravir ／ lamivudine) labels

On 11 March 2021, the FDA announced that it approved revisions to the TRIUMEQ (abacavir/dolutegravir/lamivudine) and DOVATO (dolutegravir/lamivudine) labels to include dosing in patients with creatinine clearance between 30 and 49 ml per min. Additionally, drug interaction information for TRIUMEQ and riociguat were included in the label. A summary of the major labeling changes for TRIUMEQ is below. Similar changes were made to the DOVATO label.

Section 2: DOSAGE AND ADMINISTRATION

2.5 Not Recommended Due to Lack of Dosage Adjustment

Because TRIUMEQ is a fixed-dose tablet and cannot be dose adjusted, TRIUMEQ is not recommended in patients with creatinine clearance less than 30 ml per minute.

- Section 8: USE IN SPECIFIC POPULATIONS

8.6 Patients with Impaired Renal Function

TRIUMEQ is not recommended for patients with creatinine clearance less than 30 ml per min because TRIUMEQ is a fixed-dose combination and the dosage of the individual components cannot be adjusted. If a dose reduction of lamivudine, a component of TRIUMEQ, is required for patients with creatinine clearance less than 30 ml per min, then the individual components should be used.

Patients with a creatinine clearance between 30 and 49 ml per min receiving TRIUMEQ may experience a 1.6- to 3.3-fold higher lamivudine exposure (AUC) than patients with a creatinine clearance ≥50 mL per min. There are no safety data from randomized, controlled trials comparing TRIUMEQ to the individual components in patients with a creatinine clearance between 30 and 49 ml per min who received dose-adjusted lamivudine. In the original lamivudine registrational trials in combination with zidovudine, higher lamivudine exposures were associated with higher rates of hematologic toxicities (neutropenia and anemia), although discontinuations due to neutropenia or anemia each occurred in <1% of subjects. Patients with a sustained creatinine clearance between 30 and 49 ml per min who receive TRIUMEQ should be monitored for hematologic toxicities. If new or worsening neutropenia or anemia develop, dose adjustment of lamivudine, per lamivudine prescribing information, is recommended. If lamivudine dose adjustment is indicated, TRIUMEQ should be discontinued and the individual components should be used to construct the treatment regimen.

- Section 7: DRUG INTERACTIONS

Riociguat

Abacavir: Coadministration with TRIUMEQ resulted in increased riociguat exposure, which may increase the risk of riociguat adverse reactions. The riociguat dose may need to be reduced. See full prescribing information for ADEMPAS (riociguat).

- Section 12: CLINICAL PHARMACOLOGY

Effect of Abacavir and Lamivudine on the Pharmacokinetics of Other Agents: In vitro studies have shown that abacavir has potential to inhibit CYP1A1 and limited potential to inhibit metabolism mediated by CYP3A4. Lamivudine does not inhibit or induce CYP3A4.

Abacavir, Dolutegravir, and Lamivudine: Coadministration of a single dose of riociguat (0.5 mg) to HIV-1–infected subjects receiving TRIUMEQ is reported to increase riociguat AUC(∞) compared with riociguat AUC(∞) reported in healthy subjects due to CYP1A1 inhibition by abacavir. The exact magnitude of increase in riociguat exposure has not been fully characterized based on findings from two studies.

In Hong Kong, Triumeq Tablets (HK-64012; containing abacavir/dolutegravir/lamivudine) and Dovato Tablets (HK-66511; containing dolutegravir/lamivudine) are pharmaceutical products registered by GlaxoSmithKline Limited. Both products are prescription-only medicines. As on 7 April 2021, the DH has not received any case of adverse drug reaction related to abacavir/dolutegravir/lamivudine and dolutegravir/lamivudine. In light of the above FDA's announcement, the DH issued letters to inform local healthcare professionals to draw their

attention on 12 March 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

European Union: Benefits of ifosfamide solutions continue to outweigh risks EMA's safety committee (PRAC) has concluded that the benefits of ifosfamide solutions for infusion

On 12 March 2021, EMA announced that EMA's safety committee PRAC has concluded that the benefits of ifosfamide solutions for infusion continue to outweigh their risks in the treatment of different types of cancers, including various solid tumours and blood cancers such as lymphomas (cancer of white blood cells).

The PRAC review was started because two recent studies, suggested that the risk of encephalopathy (brain disorders) with ifosfamide supplied in solution forms is higher than with the powder form. Ifosfamide-induced encephalopathy is a very common, known risk and is generally reversible. PRAC considered all available data and concluded that an increased risk of encephalopathy with ifosfamide supplied as a solution could neither be confirmed nor excluded due to limitations in the data. PRAC recommended that the existing warning on ifosfamide-induced encephalopathy in the product information should be updated with the latest information on this side effect, including its characteristics and risk factors, as well as highlighting the need to closely monitor patients.

Companies that market ifosfamide supplied as a solution will be required to carry out studies investigating the stability of the medicines in order to establish the optimal storage conditions.

Information for patients

- Encephalopathy (brain disorders) is a very common, known side effect of ifosfamide and is generally reversible. Two recent studies have suggested that the use of ifosfamide solutions may increase the risk of this side effect compared with use of the powder form. However, an in-depth review of all available data could neither confirm nor rule out this increased risk.
- The package leaflet for these medicines will be updated with the latest information on factors that may increase the risk of encephalopathy and how to recognise signs of this side effect.
- Tell your doctor immediately if you experience confusion, sleepiness, unconsciousness, hallucinations, delusions (false beliefs), blurred vision, perception disorder (difficulty understanding information provided through the senses), problems with movement such as muscle spasms or contractions, restlessness, slow or irregular movement, loss of bladder control and seizures (fits).
- Talk to your doctor before you are given an ifosfamide medicine if you have previously had treatment with another cancer medicine called cisplatin.
- Tell your doctor if you have taken medicines that affect the brain, such as those for treating or preventing vomiting and nausea, sleeping pills, opioid painkillers or allergy medicines.
- If you have any concerns about your treatment, you should discuss them with your doctor.

Information for healthcare professionals

- Administration of ifosfamide can cause encephalopathy and other neurotoxic effects; these known, very common side effects are generally reversible.
- A review of all available data on ifosfamide-induced encephalopathy concluded that an increased risk of encephalopathy with ifosfamide supplied as a solution could neither be confirmed nor ruled out due to limitations in the data.
- The existing warnings in section 4.4 (Special warnings and precautions for use) of the summary of product characteristics will be revised to include the following information:
  - Ifosfamide-induced CNS toxicity may appear within a few hours to a few days after administration and in most cases resolves within 48 to 72 hours of ifosfamide discontinuation. If CNS toxicity develops, administration of ifosfamide should be discontinued.
  - Patients should be closely monitored for symptoms of encephalopathy, in particular if patients are at increased risk for encephalopathy Symptoms may include confusion, somnolence, coma, hallucination, blurred vision, psychotic behaviour, extrapyramidal symptoms, urinary incontinence and seizures.
  - CNS toxicity seems to be dose-dependent. Risk factors for the development of ifosfamide-associated encephalopathy include hypoalbuminaemia, impaired renal

function, poor performance status, pelvic disease and previous or concomitant nephrotoxic treatments including cisplatin.

- Due to the potential for additive effects, medicines acting on the CNS (such as antiemetics, sedatives, narcotics or antihistamines) must be used with particular caution or, if necessary, be discontinued in case of ifosfamide-induced encephalopathy.

In Hong Kong, there are 4 registered pharmaceutical products containing ifosfamide. There is one registered ifosfamide product with dose form as solution for infusion and the remaining 3 products are powder for solution for infusion. All products are prescription-only medicines. As on 7 April 2021, the DH has received 14 cases of adverse drug reaction related to ifosfamide and none of them were related to encephalopathy. In light of the above EMA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 15 March 2021 and the DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

European Union: PRAC reviews signal of low levels of blood platelets with COVID-19 vaccines

On 12 March 2021, EMA announced that the EMA's safety committee PRAC has started a review of a safety signal to assess reports of immune thrombocytopenia in patients who received any of the three COVID-19 vaccines: Comirnaty, COVID-19 Vaccine AstraZeneca and COVID-19 Vaccine Moderna.

Several cases of immune thrombocytopenia (a disorder characterised by low levels of blood platelets that can lead to bruising and bleeding) were reported in the EudraVigilance database.

In the EU, enhanced safety monitoring is in place for COVID-19 vaccines to pick up reports of adverse effects, so called adverse events of special interest (AESI). Immune thrombocytopenia has been identified as an AESI after vaccination and is closely monitored by EMA, the national competent authorities and the marketing authorisation holder. After reviewing the safety reports received so far, the PRAC decided to request an in-depth review of all available data, including case reports, clinical trials and the published literature, from the respective marketing authorisation holders for these vaccines.

At this stage, it is not yet clear whether there is a causal association between vaccination and the reports of immune thrombocytopenia. These reports point to a 'safety signal' - information on new or changed adverse events that may potentially be associated with a medicine and that warrants further investigation.

PRAC will evaluate all the available data to decide if a causal relationship is confirmed or not. In cases where a causal relationship is confirmed or considered likely, regulatory action may be necessary and this usually takes the form of an update of the summary of product characteristics and the package leaflet. EMA will further communicate on the outcome of the PRAC's review.

In Hong Kong, the above product is not a registered pharmaceutical product under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

European Union: PRAC reviews signal of localised swelling related to dermal fillers with Comirnaty

On 12 March 2021, EMA announced that the EMA's safety committee PRAC has started a review of a safety signal to assess reports of localised swelling after vaccination with COVID-19 vaccine Comirnaty in people with a history of injections with dermal fillers (soft, gel-like substances injected under the skin). Skin reactions such as site itching, facial swelling and pruritus where fillers had been previously injected were initially reported by the Norwegian Medicines Agency in one patient.

A review of reports in EudraVigilance highlighted a limited number of cases of localised swelling in people with dermal fillers potentially associated with the administration of Comirnaty. After considering the available evidence, PRAC has requested from the marketing authorisation holder a review of all cases including reports, clinical trials and the published literature.

PRAC will keep investigating this signal and will

consider any regulatory action, including updating the product information of Comirnaty.

In Hong Kong, the above product is not a registered pharmaceutical product under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

European Union: PRAC concludes safety signal of anaphylaxis with COVID-19 Vaccine AstraZeneca

On 12 March 2021, EMA announced that the EMA's safety committee PRAC has recommended an update to the product information to include anaphylaxis and hypersensitivity (allergic reactions) as side effects, with an unknown frequency, and to update the existing warning to reflect that cases of anaphylaxis have been reported, following the assessment of a safety signal regarding cases of anaphylaxis (severe allergic reactions) with COVID-19 Vaccine AstraZeneca.

The update is based on a review of 41 reports of possible anaphylaxis seen among around 5 million vaccinations in the United Kingdom. After careful review of the data, PRAC considered that a link to the vaccine was likely in at least some of these cases.

Anaphylaxis is a known side effect that may occur, very rarely, with vaccines, and is already included in the risk management plan for COVID-19 Vaccine AstraZeneca as a potential risk. Therefore, the product information already contains a warning about anaphylactic reactions. This information also highlights the need for appropriate medical treatment to be readily available in case of an anaphylactic event with the vaccine, and a recommendation that people receiving the vaccine be monitored for at least 15 minutes after vaccination is already included. Any person developing such a reaction after the first dose of the vaccine should not be given a second dose. This advice, which is aligned across all the COVID-19 vaccines authorised in the EU, remains unchanged and the update to the product information does not require any change in clinical practice.

In Hong Kong, the above product is not a registered pharmaceutical product.

Australia: Approval of updated storage conditions for the Pfizer COVID-19 vaccine

On 13 March 2021, TGA announced that it has received and assessed additional data submitted by Pfizer for their COVID-19 vaccine (COMIRNATY - BNT162b2). A storage condition of - 20±5°C for up to 2 weeks (even during transportation) within the 6 month shelf life when stored at -90 to -60°C has been approved. An updated Product Information sheet is anticipated to be submitted by Pfizer and published on the TGA's website shortly.

In Hong Kong, the above product is not a registered pharmaceutical product under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). Related news was previously issued by the FDA, and was reported in the Drug News Issue No. 136. The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

Australia: AstraZeneca ChAdOx1-S COVID-19 vaccine: Reports of anaphylaxis (severe allergic reaction)

On 17 March 2021, TGA announced that it is closely reviewing reports of anaphylaxis after four cases were reported following the AstraZeneca ChAdOx1-S vaccine in the past 2 days in Queensland.

On 19 March 2021, TGA further announced that independent expert review of recently reported cases of suspected anaphylaxis following the AstraZeneca ChAdOx1-S COVID-19 vaccine has concluded that there is no increased risk of anaphylaxis associated with the vaccine above the expected rate for any other vaccine. Anaphylaxis is a very rare side effect that can occur with any vaccine.

The TGA convened a meeting of experts drawn from the TGA's Advisory Committee on Vaccines and the Australian Technical Advisory Group on Immunisation to review the individual cases in detail. The panel included medical experts in vaccine safety, infectious diseases, immunology,

epidemiology and social science. On 18 Mar 2021, the panel reviewed the five reports and information on two additional cases of suspected anaphylaxis following the AstraZeneca COVID-19 vaccine received by the TGA. Four reports came from Queensland and one from each of Victoria, New South Wales (NSW) and Northern Territory. The panel found that the information in only one of the reports met the required assessment criteria for anaphylaxis. This individual made a full recovery. In considering the reports, the panel used the internationally-accepted Brighton Collaboration case definition of anaphylaxis. The panel advised that some of these cases may have represented allergic reactions or immediate stress responses to vaccination that may appear similar to an anaphylactic reaction, with symptoms such as nausea, throat tightness or rapid heart rate. Although they might not meet the criteria for anaphylaxis, they still need to be monitored and taken seriously.

In addition to the advice provided in the statement published on 17 Mar 2021, which is still relevant and applicable, the TGA recommends that immunisation providers continue to provide adrenaline where they feel it is clinically required.

In Hong Kong, the above product is not a registered pharmaceutical product.

Canada: Summary Safety Review: Remicade (infliximab), Humira (adalimumab), Enbrel (etanercept) and Erelzi (biosimilar etanercept): Assessing the potential risk of mycosis fungoides

On 18 March 2021, Health Canada announced that it reviewed the potential risk of mycosis fungoides in patients treated with Tumor Necrosis Factor (TNF) alpha-blockers (or anti-TNF alpha) products following the publication, in the World Health Organization (WHO) Pharmaceutical Newsletter, of mycosis fungoides cases resulting from the administration of infliximab (Remicade) reported by the Australian Therapeutic Goods Administration.

Mycosis fungoides is a type of cancer involving white blood cells, called T-lymphocytes, which grow out of control in the skin. It is a form of cutaneous T-cell lymphoma.

Health Canada's review of information received from the manufacturers and published literature concluded that a link between mycosis fungoides and the use of anti-TNF alpha products could not be confirmed due to limitations in the cases assessed. Mycosis fungoides is a form of lymphoma, which is already included in the Canadian Product Monograph of anti-TNF alpha products.

Health Canada's review of the available information concluded that a link between the risk of mycosis fungoides, a type of lymphoma, and the use of anti-TNF alpha products could not be confirmed given limitations in the available information. As the product safety information for all anti-TNF alpha products already mentions the risk of lymphoma (which includes mycosis fungoides), no updates specific for mycosis fungoides are required at this time.

In Hong Kong, there are registered pharmaceutical products containing infliximab (3 products), adalimumab (6 products) and etanercept (4 products). All products are prescription-only medicines. As of 7 April 2021, the DH has received adverse drug reaction related to infliximab (13 cases), adalimumab (15 cases) and etanercept (11 cases), but these cases are not related to mycosis fungoides. The local product information of the above products already include the risk of lymphoma. The DH will remain vigilant on safety update of the drugs issued by other overseas drug regulatory authorities.

Canada: Summary Safety Review - Diuretics, Including Acetazolamide - Assessing the Potential Risk of Certain Eye Disorders

On 19 March 2021, Health Canada announced that it reviewed the potential risks of choroidal effusion (CE), acute myopia (AM) and acute angle-closure glaucoma (AACG) with the use of diuretics, including acetazolamide. The safety review was triggered by updates made by the European Medicines Agency to include these risks in the product safety information for certain diuretics.

At the time of the review, the Canadian product safety information for some diuretics included information related to one or all of these eye disorders. The purpose of this review was to assess if additional actions were required for diuretics marketed in Canada.

Diuretics are prescription drugs authorized for sale in Canada to treat various medical conditions, but are mainly used to reduce swelling caused by a

build up of body fluids (edema) and to lower high blood pressure. Acetazolamide is authorized for sale in Canada to treat increased pressure in the eye (glaucoma), certain types of seizures and overdose from acetylsalicylic acid (ASA). Acetazolamide for Injection is also authorized to treat edema.

Health Canada reviewed the available information from searches of the Canada Vigilance database, international databases and published literature.

Health Canada reviewed 49 cases (1 Canadian, 48 foreign) of choroidal effusion, acute myopia or acute angle-closure glaucoma with the use of diuretics, including acetazolamide. The 48 foreign cases included 7 reported to the Canada Vigilance database and 41 that were only available through the scientific literature.

Health Canada's review found a link between the unlikely to be linked. For furosemide, 1 case was found to be possibly linked, 2 cases were not likely to be linked and 1 case did not have enough information to be assessed. Of the 19 acetazolamide cases reviewed, 1 case was found to be probably linked, 12 cases were possibly linked, 1 case was unlikely to be linked and 5 cases could not be assessed. The remaining 5 cases were considered unlikely to have a link (spironolactone, triamterene, methyclothiazide, azosemide) or did not have enough information to be assessed (xipamide).

At the time of the review, no information was found to support a link between Zaroxolyn (metolazone) and the risk of eye disorders. However, given the similar chemical structure of Zaroxolyn to chlorthalidone and indapamide, the risks of CE, AM or AACG with Zaroxolyn use could not be excluded.

While the published literature supported a link between the risks of CE, AM or AACG with certain diuretics, including acetazolamide, it did not identify a clear biological mechanism to explain how diuretics, including acetazolamide, could lead to these eye disorders.

Health Canada's review of the available information showed a link between the use of certain diuretics, namely products containing hydrochlorothiazide, chlorthalidone, indapamide and acetazolamide, and the risks of CE with AM or with AACG or with both AM and AACG. In addition, Health Canada's review concluded that there might be a link between Zaroxolyn and the risk of these eye disorders.

Health Canada will work with manufacturers to update the Canadian product safety information for products containing hydrochlorothiazide, chlorthalidone, indapamide and acetazolamide as well as Zaroxolyn to add a warning about the risks of CE with AM or with AACG or with both AM and AACG. 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 diuretics, including acetazolamide-containing products.

In Hong Kong, there are registered pharmaceutical products containing hydrochlorothiazide (105 products), chlorthalidone (5 products), indapamide (29 products) and acetazolamide (3 products). All products are prescription-only medicines. There is no registered pharmaceutical product containing metolazone. As on 7 April, the DH has received adverse drug reaction related to hydrochlorothiazide (7 cases) and indapamide (1 case), but these cases are not related to eye disorders. DH has received 1 case of adverse drug reaction with increased intraocular pressure related to acetazolamide. In light of the above Health Canada's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 22 March 2021 and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Macao: Defects found in packaging of the mRNA COVID-19 vaccine manufactured by BioNTech. Macao has suspended vaccination of this vaccine from today (24 March 2021)

On 24 March 2021, the Macao Health Bureau announced that it has received a written notification from Fosun Pharma that a number of packaging defects on the closure of the mRNA COVID-19 vaccine Comirnaty® manufactured by BioNTech of Germany with batch number 210102 (expiry 06/2021) were recently noticed. BioNTech and Fosun Pharma have initiated an investigation to identify the root cause of the problem and vaccination has to be suspended immediately. All the mRNA vaccines procured by Macao belong to the above batch, and vaccination should be suspended with immediate effect today until further notice.

The Macao Health Bureau further announced that it has held a meeting with Fosun Pharma on 24 March to follow up on the incident.

On 27 March 2021, the Macao Health Bureau announced that it has received notification from Fosun Pharma that, based on the investigation conducted so far, there are no obvious systematic factors found from the vaccine packaging process to administration that may have attributed to the defects. The current stage of investigation cannot rule out the possibility of environmental factors during long-haul transportation. The follow-up investigations of Fosun Pharma and BioNTech will be conducted mainly on the verification of the inherent characteristics of the relevant batch of vaccine and that they can be used safely; and the investigation process is intended to be completed within one week.

In Hong Kong, the COVID-19 vaccine by Fosun Pharma /BioNTech (i.e. Comirnaty) is authorised for emergency use in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). The importer of the vaccine confirmed that a total of two batches (batch numbers: 210102 and 210104) were imported into Hong Kong.

The DH had earlier noticed that there was an accumulated number of cases of packaging defects (including loose vial caps, leakages from the vials, etc.) regarding the BioNTech vaccines (batch number: 210102). The DH immediately notified the vaccine supplier (Fosun Industrial Co., Limited (Fosun) and German drug manufacturer BioNTech) and requested for prompt follow-up. At the same time, in view that the supplier has launched an urgent and comprehensive investigation on the packaging defects, the Government agreed to the supplier's recommendation and suspended vaccination of batch 210102 and 210104 of the BioNTech vaccines in Hong Kong for the sake of prudence and as a precautionary measure.

On 27 March 2021, the Government announced that the initial investigation results was received from Fosun. According to the investigations completed by Fosun and BioNTech so far, there is no indication of any obvious systematic factors during the processes from filling and packaging to administration that could have led to the relevant packaging defects. At this juncture, the investigation results do not rule out that the relevant situation is caused by environmental conditions during the long-haul transport process. That said, having regard to consolidated figures from the investigation, it is believed that the relevant situation is not related to cold-chain and logistical management. As regards the other vaccine doses which were delivered to Hong Kong, random sample testing of vaccine vials which are intact did not uncover any issue of vaccine leakage.

According to the initial investigation results, Fosun and German drug manufacturer BioNTech considered that there is no evidence indicating any safety risks of the BioNTech vaccines delivered to Hong Kong (batch numbers: 210102 and 210104). The subsequent investigation work will mainly target on ascertaining the integrity of the intrinsic properties of the relevant batches of vaccine, and that the batches are safe for use. The Government is actively following up with Fosun and German manufacturer BioNTech to strive to complete the investigation procedures within a week.

The DH will continue to monitor the incident for consideration of any action deemed necessary, and will timely announce the latest situation and arrangement as soon as possible.

The United States: FDA requires a warning about Guillain-Barré Syndrome (GBS) be included in the Prescribing Information for Shingrix

On 24 March 2021, the FDA announced that it has required and approved safety labeling changes to the Prescribing Information for Shingrix (Zoster Vaccine Recombinant, Adjuvanted) to include a new warning about the risk for Guillain-Barré Syndrome (GBS) following administration of Shingrix. FDA required GlaxoSmithKline (GSK), the manufacturer of Shingrix, to revise the Prescribing Information to include the following language in the Warnings and Precautions section:

- In a postmarketing observational study, an increased risk of GBS was observed during the 42 days following vaccination with Shingrix.

FDA evaluated data from a postmarketing observational study that assessed the risk of GBS following vaccination with Shingrix. Based on this evaluation, FDA has determined that the results of this observational study show an association of GBS with Shingrix, but that available evidence is insufficient to establish a causal relationship.

The Centers for Disease Control and Prevention (CDC) conducted postmarketing safety surveillance of Shingrix in the Vaccine Safety Datalink (VSD) by monitoring prespecified adverse events, including GBS, among individuals 50 years of age and older who received Shingrix. The VSD analyses identified a preliminary statistical signal suggesting an increased risk of GBS among individuals who received Shingrix compared to a historical control group of individuals who had received Zostavax (Zoster Vaccine Live), another FDA-approved vaccine for the prevention of shingles. To evaluate this statistical signal, FDA, the Centers for Medicare & Medicaid Services (CMS), and CDC investigated GBS risk following administration of Shingrix in the Medicare claims database. This is the largest postmarket study evaluating GBS risk following vaccination with Shingrix.

The association between vaccination with Shingrix and GBS was evaluated among Medicare beneficiaries aged 65 years or older. Using Medicare claims data, from Oct 2017 through Feb 2020, 3,729,863 vaccinations with Shingrix (administered to 2,113,758 Medicare beneficiaries) were identified through National Drug Codes, and potential cases of hospitalized GBS among recipients of Shingrix were identified through International Classification of Diseases codes.

The risk of GBS following vaccination with Shingrix was assessed in self-controlled case series analyses using a risk window of 1 to 42 days post-vaccination and a control window of 43 to 183 days post-vaccination. The primary analysis (claims-based, all doses) found an increased risk of GBS during the 42 days following vaccination with Shingrix, with an estimated 3 excess cases of GBS per million doses administered to adults aged 65 years or older. In secondary analyses, an increased risk of GBS was observed during the 42 days following the first dose of Shingrix, with an estimated 6 excess cases of GBS per million doses administered to adults aged 65 years or older, and no increased risk of GBS was observed following the second dose of Shingrix. These analyses of GBS diagnoses in claims data were supported by analyses of GBS cases confirmed by medical record review.

FDA evaluated data from the above study, and based on this evaluation, FDA has determined that the results of this observational study show an association of GBS with Shingrix, but that available evidence is insufficient to establish a causal relationship. FDA has concluded that revision to the Warnings and Precautions section of the Prescribing Information for Shingrix to include a warning about GBS is warranted. FDA has determined that the benefits of vaccination with Shingrix continue to outweigh its risks.

In Hong Kong, Shingrix Vaccine Powder And Suspension For Suspension For Injection (HK-66840) is a pharmaceutical product registered by GlaxoSmithKline Limited, and is a prescription-only medicine. As on 7 April 2021, the DH has not received any case of adverse drug reaction related to Shingrix. In light of the above FDA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 25 March 2021 and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

The United Kingdom: Bendamustine (Levact): increased risk of non-melanoma skin cancer and progressive multifocal encephalopathy (PML)

On 24 March 2021, MHRA announced an increased risk of non-melanoma skin cancer and progressive multifocal encephalopathy (PML) associated with the use of bendamustine.

Patients treated with bendamustine have an existing increased risk for non-melanoma skin cancer due to their underlying disease and age. However, two published trials (BRIGHT and GALLIUM) show a higher number of cases of non-melanoma skin cancer with bendamustine-containing regimens than with other treatments used for lymphoma. A European review of safety data has recommended these risks be added to the Summary of Product Characteristics alongside advice to periodically monitor patients for skin changes. Advice will also be added to the Patient Information Leaflet to state that patients should contact their doctor if they notice worrying skin changes.

In addition, very rare cases of PML have been reported in patients on bendamustine-containing regimens. Although concomitant treatment was present in all cases where information was provided, a temporal relationship with bendamustine was evident in most cases and an increased risk of PML is thought plausible. These risks have been added to the product information and patients should be directed to the patient information leaflet to be aware of signs and

symptoms of PML. If PML is suspected, treatment with bendamustine should be suspended until PML is ruled out. Evaluation of PML includes, but is not limited to, brain magnetic resonance imaging (MRI), and lumbar puncture (cerebrospinal fluid testing for John Cunningham viral DNA).

The BRIGHT trial is a completed, phase 3, open-label, randomised, parallel-group study of first-line treatments for patients with advanced indolent non-Hodgkin's lymphoma or mantle cell lymphoma. The trial compared outcomes in patients assigned to bendamustine plus rituximab versus alternative chemotherapy regimens (R-CHOP/R-CVP). In this trial, 14 of 221 (6.3%) patients treated with bendamustine plus rituximab and 5 of 215 (2.3%) patients treated with R-CHOP/R-CVP were reported to develop squamous cell carcinoma or basal cell carcinoma.

The GALLIUM trial was an open-label, randomised parallel-group study of previously untreated follicular lymphoma (grade 1 to 3a; stage III or IV disease). The trial compared outcomes in patients randomised to receive either obinutuzumab or rituximab plus a chemotherapy backbone with bendamustine or alternative chemotherapy regimens (R-CHOP/R-CVP). This study took into account all malignancies occurring more than 6 months after first study drug intake. Basal cell carcinoma was reported in 16 of 676 patients (2.4%) receiving bendamustine versus 1 of 513 patients receiving CHOP/CVP. There were also increases in the number of reports of squamous cell carcinoma in patients receiving bendamustine, while no cases were reported in patients receiving CHOP/CVP.

The European review of safety data also identified an increase in reporting of cases of PML when bendamustine-containing therapy is used. During the period reviewed (7 Jan 2018 to 6 Jan 2020), 42 cases of PML worldwide were reported, 11 of which were fatal. This compared to 9 cases in the previous period (7 Jan 2017 to 6 Jan 2018). Concomitant treatment was present in all cases, with most receiving rituximab or obinutuzumab alongside bendamustine. However, a temporal relationship with bendamustine was evident in most cases. In 31 of the cases, bendamustine-containing therapy was the latest treatment before onset. A contributory role of bendamustine to the development of PML is thought possible. It is known that bendamustine can cause prolonged lymphopenia and CD4-positive T-cell depletion. This effect is more pronounced when bendamustine is combined with rituximab.

Advice for healthcare professionals:

- In clinical studies, an increased risk from background for non-melanoma skin cancers (basal cell carcinoma and squamous cell carcinoma) has been observed in patients treated with bendamustine-containing therapies.
- Periodically perform skin examinations in patients on bendamustine-containing regimens, particularly in patients with risk factors for skin cancer – these include people with lighter natural skin colour; skin that burns, freckles or reddens easily; a large number of moles; and a personal or family history of skin cancer.
- Very rare cases of PML have also been reported in patients being treated with bendamustine usually in combination with rituximab or obinutuzumab.
- Consider PML in the differential diagnosis for patients on bendamustine with new or worsening neurological, cognitive, or behavioural signs or symptoms.
- If PML is suspected, undertake appropriate diagnostic evaluations and suspend treatment until PML is excluded.

In Hong Kong, there are 6 registered pharmaceutical products containing bendamustine. All products are prescription-only medicines. As on 7 April 2021, the DH has received 21 cases of adverse drug reaction related to bendamustine, but these cases are not related to non-melanoma skin cancer and progressive multifocal encephalopathy. In light of the above MHRA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 25 March 2021 and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

European Union: New manufacturing site and more flexible storage conditions for BioNTech ／ Pfizer's COVID-19 vaccine

On 26 March 2021, EMA announced that a new site has also been approved for the production of Comirnaty, the COVID-19 vaccine developed by BioNTech and Pfizer. The facility, which is in the German city of Marburg, will produce both active substance and the finished product. There are currently three active substance manufacturing sites

supplying the EU included in the marketing authorisation.

In addition to the new manufacturing facility for this vaccine, the CHMP has also given a positive opinion to allow transportation and storage of vials of this vaccine at temperatures between -25 to -15˚C (i.e. the temperature of standard pharmaceutical freezers) for a one-off period of two weeks. This is an alternative to the long-term storage of the vials at a temperature between -90 to -60˚C in special freezers. It is expected to facilitate the rapid roll-out and distribution of the vaccine in the EU by reducing the need for ultra-low temperature cold storage conditions throughout the supply chain.

In Hong Kong, the above product is not a registered pharmaceutical product under the Pharmacy and Poisons Ordinance (Cap. 138). The COVID-19 vaccine by Fosun Pharma/BioNTech (i.e. Comirnaty) is authorised for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). Related news was previously issued by the FDA, and was reported in the Drug News Issue No. 136. The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

Singapore: Risk of major adverse cardiovascular events and malignancies (excluding non-melanoma skin cancer) with use of Xeljanz (tofacitinib) relative to tumour necrosis factor inhibitors

On 29 March 2021, Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Pfizer to inform healthcare professionals of preliminary results from a safety clinical trial which found an increased risk of major adverse cardiovascular events and malignancies (excluding non-melanoma skin cancer) with Xeljanz, compared with tumor necrosis factor inhibitors. Pfizer is working with regulatory agencies to review the full results and analyses as they become available. In addition, Pfizer is conducting additional analyses to further identify any risk factors that might have contributed to the increased risk, which will inform the need for any additional risk mitigation measures.

Healthcare professionals are advised to consider the benefits and risks of Xeljanz when deciding whether to prescribe or continue patients on the medicine and to continue to follow the recommendations in the Xeljanz prescribing information. Healthcare professionals are also recommended to counsel their patients about the risks and benefits of Xeljanz and to advise them not to stop taking Xeljanz without consulting their healthcare professional.

In Hong Kong, there are 3 registered pharmaceutical products containing tofacitinib, namely Xeljanz Tablets 5mg (HK-63303), Xeljanz XR Extended Release Tablets 11mg (HK-66141) and Xeljanz Tablets 10mg (HK-66833). All products are registered by Pfizer Corporation Hong Kong Limited, and are prescription-only medicines. As on 7 April 2021, the DH has received 8 cases of adverse drug reaction related to tofacitinib, of which one case is related to lung cancer.

Related news was previously issued by the FDA, and was reported in the Drug News Issue No. 136. As the review is ongoing, the DH will remain vigilant on its final conclusions and recommendations, and safety update issued by FDA, HSA and other overseas drug regulatory authorities for consideration of any action deemed necessary.

The United States: Studies show increased risk of heart rhythm problems with seizure and mental health medicine lamotrigine (Lamictal) in patients with heart disease

On 31 March 2021, the FDA announced that a FDA review of study findings showed a potential increased risk of heart rhythm problems, called arrhythmias, in patients with heart disease who are taking the seizure and mental health medicine lamotrigine (Lamictal). FDA wants to evaluate whether other medicines in the same drug class have similar effects on the heart and is requiring safety studies on those also. FDA will update the public when additional information from these studies becomes available.

FDA required these studies, called in vitro studies, to further investigate Lamictal's effects on the heart after FDA received reports of abnormal electrocardiographic (ECG) findings and some other serious problems. In some cases, problems including chest pain, loss of consciousness, and cardiac arrest occurred. In vitro studies are studies done in test tubes or petri dishes and not in people or animals. FDA first added information about this risk to the lamotrigine prescribing information and

Safety Update

Medication Guides in Oct 2020, which FDA has updated.

Patients should not stop taking their medicine without first talking to their prescriber because stopping lamotrigine can lead to uncontrolled seizures, or new or worsening mental health problems. Contact their health care professional right away or go to an emergency room if they experience an abnormal heart rate or irregular rhythm, or symptoms such as a racing heartbeat, skipped or slow heartbeat, shortness of breath, dizziness, or fainting.

Health care professionals should assess whether the potential benefits of lamotrigine outweigh the potential risk of arrhythmias for each patient. Laboratory testing performed at therapeutically relevant concentrations has shown that lamotrigine can increase the risk of serious arrhythmias, which can be life-threatening, in patients with clinically important structural or functional heart disorders. Clinically important structural and functional heart disorders include heart failure, valvular heart disease, congenital heart disease, conduction system disease, ventricular arrhythmias, cardiac channelopathies such as Brugada syndrome, clinically important ischemic heart disease, or multiple risk factors for coronary artery disease. The risk of arrhythmias may increase further if used in combination with other medicines that block sodium channels in the heart. Other sodium channel blockers approved for epilepsy, bipolar disorder, and other indications should not be considered safer alternatives to lamotrigine in the absence of additional information.

In Hong Kong, there are 26 registered pharmaceutical products containing lamotrigine. All products are prescription-only medicines. As on 7 April 2021, the DH has received 2 cases of adverse drug reaction related to lamotrigine, but these cases are not related to arrhythmias. In light of the above FDA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 1 April 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Incident

Public urged not to buy or consume slimming product with undeclared banned ingredient

On 9 March 2021, the DH appealed to members of the public not to buy or consume a slimming product named "Blackruby_shop" as it was found to contain an undeclared and banned Western drug ingredient that might be dangerous to health.

Upon intelligence, a local seller was found offering for sale the above slimming product via a social media platform. Samples of the product were obtained for analysis and the Government Laboratory's results confirm that the samples contained sibutramine, a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138) (the Ordinance). The DH's investigation is continuing.

Sibutramine was once used as an appetite suppressant. Since November 2010, products containing sibutramine have been banned in Hong Kong because of an increased cardiovascular risk.

Press release was posted on the Drug Office website on 9 March 2021 to alert the public of the drug incident.

Public urged not to buy or consume slimming product with undeclared Western drug ingredient

On 17 March 2021, the DH appealed to the public not to buy or consume a slimming product named LKS Coffee as it was found to contain an undeclared and banned drug ingredient that might be dangerous to health.

Acting upon intelligence, a sample of the above product was purchased via a social media network platform for analysis. The test result from the Government Laboratory revealed that the sample contained a banned drug ingredient, sibutramine. The DH's investigation is continuing.

Sibutramine is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138). It was once used as an appetite suppressant. Since November 2010, pharmaceutical products containing sibutramine have been banned in Hong Kong because of increased cardiovascular risk.

Press release was posted on the Drug Office website on 17 March 2021 to alert the public of the drug incident.

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 $30,000 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.

All registered pharmaceutical products should carry a Hong Kong registration number on the package in the format of "HK-XXXXX". The products mentioned in the above incidents were not registered pharmaceutical products under the Ordinance in Hong Kong. Their safety, quality and efficacy cannot be guaranteed. Members of the public were exhorted not to use products of unknown or doubtful composition. They should stop using the aforementioned products immediately if they had them in their possession and to consult healthcare professionals if they felt unwell after taking the products. The products should be destroyed or disposed properly, or submitted to the Department's Drug Office during office hours.

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.

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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.