Drug News
藥 物 情 報

Issue Number 135

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in January 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: Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-norepinephrine Reuptake Inhibitors (SNRIs): Assessing the potential risk of sexual dysfunction despite treatment discontinuation

On 6 January 2021, Health Canada announced that it reviewed the potential risk of persistent or worsening sexual dysfunction, as well as the appearance of new symptoms of sexual dysfunction after stopping Selective Serotonin Reuptake Inhibitor (SSRI) or Serotonin-norepinephrine Reuptake Inhibitor (SNRI) treatment. The safety review was triggered by information received from the European Medicines Agency (EMA), which was contacted by a group of physicians and scientists concerned that stopping SSRI or SNRI treatment could result in persistent, worsening, or new symptoms of sexual dysfunction. It is well known that continued treatment with SSRIs and SNRIs can cause sexual problems (dysfunction) such as low sexual desire, problems maintaining an erection, orgasm problems, genital or nipple numbness, etc.

In Canada, SSRIs authorized for use include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vilazodone and vortioxetine, and SNRIs authorized for use include desvenlafaxine, duloxetine, levomilnacipran and venlafaxine.

Health Canada reviewed information from published and unpublished population-based (epidemiologic) studies and case reports of individual patients. Information was obtained from searches of international databases of published literature, drug manufacturers, physicians concerned about this issue, as well as searches of the Canada Vigilance database. Epidemiologic studies reporting sexual dysfunction with SSRIs or SNRIs use were not specifically designed to assess a link between treatment discontinuation and persistent, worsening, or new symptoms of sexual dysfunction, so were not included because of concerns about the accuracy of their findings.

Health Canada's review of case reports focused on the outcome of persistent sexual dysfunction. Existing assessment tools were not designed to assess the link between treatment discontinuation and changes in patient symptoms (such as worsening of existing symptoms, or the appearance of new symptoms of sexual dysfunction). Of the 58 case reports of sexual dysfunction, 43 cases (16 Canadian, 27 international) of persistent sexual dysfunction were considered possibly linked to previous use and discontinuation of SSRI or SNRI treatment. The remaining 15 cases could not be assessed because there was not enough information. In some of these case reports, symptoms lasted long after treatment discontinuation (weeks to years).

Health Canada's review could not confirm, nor rule out, a causal link between stopping SSRI or SNRI treatment and persistent sexual dysfunction. Health Canada's review could not make conclusions about worsening or new symptoms of sexual dysfunction as the studies were not designed to assess this. Health Canada will work with manufacturers to update the product safety information for all SSRIs and SNRIs to recommend that healthcare professionals inform patients about the potential risk of long lasting (possibly weeks to years) sexual symptoms persisting after stopping SSRI or SNRI treatment.

In Hong Kong, there are registered pharmaceutical products containing SSRIs and SNRIs, including citalopram (15 products), escitalopram (33 products), fluoxetine (23 products), fluvoxamine (4 products), paroxetine (11 products),

sertraline (21 products), vortioxetine (3 products), desvenlafaxine (3 products), duloxetine (12 products), milnacipran (2 products) and venlafaxine (31 products). All products are prescription-only medicines. There is no registered pharmaceutical product containing vilazodone and levomilnacipran.

As on 5 February 2021, the Department of Health (DH) has received adverse drug reaction (ADR) related to citalopram (one case), escitalopram (2 cases), fluoxetine (one case), sertraline (2 cases), vortioxetine (3 cases), desvenlafaxine (9 cases), duloxetine (one case) and venlafaxine (3 cases), but these cases are not related to sexual dysfunction. The DH has not received any case of ADR related to fluvoxamine, paroxetine and milnacipran.

In light of the above Health Canada's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 7 January 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board (Registration Committee).

UK: SSRI ／ SNRI antidepressant medicines: small increased risk of postpartum haemorrhage when used in the month before delivery

On 7 January 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) announced that data from observational studies suggest that the use of SSRI/SNRI antidepressants during the month before delivery may result in a small increased risk of postpartum haemorrhage.

SSRIs and SNRIs are two classes of commonly used antidepressant medicines. These medicines have been known for some time to increase the general risk of bleeding. This is thought to be due to serotonergic effect impairing platelet aggregation. Bleeding abnormalities associated with use of these medicines have been reported rarely and the absolute risk is thought to be low.

A recent European Union (EU) review considered spontaneous data in the context of a wider literature review for SSRI and SNRI medicines. The review identified observational studies reporting an increased risk of postpartum haemorrhage in association with antidepressant use in late pregnancy, particularly for SSRIs and SNRIs. Despite heterogeneous data and differences in definitions of postpartum haemorrhage, the review concluded that the data suggested a slightly increased risk of postpartum bleeding with use of SSRIs and SNRIs during the month before delivery. The review concluded that this risk might also apply to the newest antidepressant vortioxetine. Following the review, warnings are being added to the product information for these medicines (list of products below) to advise that they may increase the risk of postpartum haemorrhage.

Rates of postpartum haemorrhage vary by geographical region with one study suggesting rates in Europe of 12.7% with a blood loss greater than 500 millilitres and 2.8% with a blood loss greater than 1000 millilitres. The review estimated that the use of antidepressant medicines in the month before delivery increases the risk by less than two-fold. The severity of cases was not reported, but no fatalities were flagged in the dataset reported by the European review. Some datasets in the meta-analyses considered in the review defined all postpartum haemorrhage as blood loss of 500 millilitres or higher; some as 1000 millilitres. Although the added risk of postpartum haemorrhage related to use of SSRI/SNRI antidepressants is small, it may be significant in individual patients when combined with other risk factors for post-partum haemorrhage. Updates to the patient information leaflets will include the increased risk, especially for patients with bleeding disorders. The leaflets will advise that the midwife or doctor should be made aware they are taking these medicines.

In the UK, the MHRA has received a very small number of suspected ADRs reporting postpartum haemorrhage in association with antidepressant medicines.

The Commission on Human Medicines (CHM) ' Medicines in Women's Health Expert Advisory Group (MWHEAG) has considered the review findings and advised on the need to make healthcare professionals aware of the potential increased risk of bleeding in women who take SSRI/SNRI antidepressants in the month before delivery. They advised that these risks should be incorporated into the standard clinical risk assessment for bleeding and thrombotic risk. MWHEAG advised that prescribers should encourage compliance with heparin self-administration in all patients with risk factors for venous thromboembolism. Clinical experience

suggests approximately one-third of patients require heparin in the postpartum period after caesarean section to reduce the risk of venous thromboembolic events. The benefits and risk of all medicines should be carefully considered, and the new data carefully communicated in the context of the risk of thromboembolic events. Thromboembolic events in the peripartum period can have potentially fatal consequences. Women who have been prescribed heparin should be encouraged to adhere closely to the recommended dose and frequency of administration of heparin as advised by their doctor even if they are also taking SSRI or SNRIs.

Taking the evidence into account, the review considered there to be sufficient evidence to update the product information for:

- SSRIs: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline;
- SNRIs: desvenlafaxine, milnacipran, venlafaxine;
- Vortioxetine.

Advice for healthcare professionals:

- SSRIs and SNRIs are known to increase the bleeding risk; observational data suggest that the use of some antidepressants in the last month before delivery may increase the risk of postpartum haemorrhage.
- Continue to consider the benefits and risks for use of antidepressants during pregnancy, and the risks of untreated depression in pregnancy.
- Healthcare professionals, including midwives, should continue to enquire about the use of antidepressant medicines, particularly in women in the later stages of pregnancy.
- Consider the findings of the review in the context of individual patient risk factors for bleeding or thrombotic events.
- Do not stop anticoagulant medication in women at high risk of thrombotic events in reaction to these data but be aware of the risk identified.

In Hong Kong, there are registered pharmaceutical products containing SSRIs and SNRIs, including citalopram (15 products), escitalopram (33 products), fluoxetine (23 products), fluvoxamine (4 products), paroxetine (11 products), sertraline (21 products), vortioxetine (3 products), desvenlafaxine (3 products), duloxetine (12 products), milnacipran (2 products) and venlafaxine (31 products). All products are prescription-only medicines.

As on 5 February 2021, the DH has received ADR related to citalopram (one case), escitalopram (2 cases), fluoxetine (one case), sertraline (2 cases), vortioxetine (3 cases), desvenlafaxine (9 cases), duloxetine (one case) and venlafaxine (3 cases), but these cases are not related to postpartum haemorrhage. The DH has not received any case of ADR related to fluvoxamine, paroxetine and milnacipran.

In light of the above MHRA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 8 January 2021 and the matter will be discussed by the Registration Committee.

UK: Fingolimod (Gilenya▼): updated advice about the risks of serious liver injury and herpes meningoencephalitis

On 7 January 2021, the MHRA announced that liver monitoring requirements and discontinuation criteria for fingolimod have been updated following reports of serious liver injury. Fatal cases of encephalitis and meningitis caused by herpes simplex and varicella zoster viruses have been reported during treatment.

A recent European review of safety data identified 7 cases of clinically significant liver injury that developed between 10 days and 5 years after the start of fingolimod treatment, including 3 post-marketing reports of acute hepatic failure requiring liver transplantation. Liver samples showed submassive hepatic necrosis in 2 patients, and one of these samples also contained features of acute hepatitis. The MHRA has not received any UK reports via the Yellow Card scheme of acute hepatic failure or serious liver injury (defined as serum aspartate aminotransferase, AST, or serum alanine aminotransferase, ALT, at 3-times upper limit of normal, ULN, or higher with increased bilirubin or jaundice) considered causally related to fingolimod treatment. Due to the severity of recently reported cases, recommendations for liver monitoring and the discontinuation criteria have been strengthened to minimise the risks of liver injury.

Advice in the product information regarding the risks of herpes zoster/herpes simplex infections with fingolimod has also been updated following the review's consideration of reported cases of infections with visceral or central nervous system (CNS) dissemination, some of which were fatal.

Remind patients to seek immediate medical attention if they have a fever or signs of infection (including influenza or shingles) or if they have symptoms of meningitis or encephalitis during fingolimod treatment and up to 2 months after the last dose.

The product information and the educational materials in the UK will be revised to include updated advice for healthcare professionals and patients on the risks of serious liver injury and of herpes meningoencephalitis and cryptococcal meningitis.

Advice for healthcare professionals:

- A small number of cases of clinically significant liver injury, including acute hepatic failure requiring transplantation, have been reported during fingolimod treatment.
- Monitor liver function tests (including bilirubin) routinely: before starting treatment; during treatment at months 1, 3, 6, 9 and 12; and then periodically until 2 months after discontinuation.
- In patients without signs and symptoms of liver injury, the updated advice is:
  - monitor liver function tests more frequently if AST or ALT levels exceed 3-times the ULN but less than 5-times ULN with a normal bilirubin level;
  - discontinue fingolimod if ALT or AST levels exceed 5-times ULN or if they are at least 3-times the ULN and bilirubin is increased – fingolimod may be re-started following a careful benefit-risk assessment of the underlying cause when serum levels have returned to normal.
- In patients with symptoms or signs of hepatic dysfunction:
  - check liver function tests urgently;
  - discontinue fingolimod if significant hepatic injury is confirmed; further treatment with fingolimod may be considered following recovery only if an alternative cause of hepatic dysfunction is established.

- Continue to be vigilant for infections with fingolimod; information has been updated to include herpes zoster/herpes simplex infections with visceral or CNS dissemination.

In Hong Kong, there are 3 registered pharmaceutical products containing fingolimod, namely Gilenya Hard Capsules 0.5mg (HK-61192) and Gilenya Hard Capsules 0.25mg (HK-66472) which are registered by Novartis Pharmaceuticals (HK) Limited; and Fingolimod Teva Capsules 0.5mg (HK-66882) which is registered by Teva Pharmaceutical Hong Kong. All products are prescription-only medicines. As on 5 February 2021, the DH has received 14 cases of ADR related to fingolimod, but these cases are not related to liver injury and herpes meningoencephalitis.

Related news on the risk of infections (including central nervous system infections caused by herpes simplex and varicella zoster viruses) and liver injury (with strengthening of recommendations for liver monitoring and the discontinuation criteria) was previously issued by the MHRA and Taiwan Food and Drug Administration (TFDA), and was reported in the Drug News Issue No. 78 and 134. The DH issued letters to inform local healthcare professionals to draw their attention on 19 April 2016 and 16 December 2020. In light of the above MHRA's announcement, the matter will be discussed by the Registration Committee.

UK: Dimethyl fumarate (Tecfidera): updated advice on the risk of progressive multifocal leukoencephalopathy (PML) associated with mild lymphopenia

On 7 January 2021, the MHRA announced a small number of reports of progressive multifocal leukoencephalopathy (PML) in patients with mild lymphopenia treated with dimethyl fumarate.

A recent European review of safety data identified 11 cases of PML with lymphopenia associated with Tecfidera treatment, including 3 cases in patients with mild lymphopenia (lymphocyte counts defined as lymphocyte counts between $0.8x10^9$ per litre and the lower limit of normal [per local laboratory]). These reports were received within an estimated exposure to Tecfidera of more than 475,000 patients.

The risk of PML in patients with mild lymphopenia has been added to the product information (Summary of Product Characteristics, SmPC), alongside a new contraindication for suspected or confirmed PML.

The MHRA has not received any UK reports via the Yellow Card scheme of confirmed PML cases associated with Tecfidera.

Lymphocyte counts should be checked before starting Tecfidera and continue to be monitored

routinely every 3 months during treatment. Lymphocyte counts and neurological symptoms should be monitored more closely in patients with lymphopenia. Prescribers should be aware that the following factors may further increase the risk of PML in individuals with lymphopenia:

- duration of treatment – PML has been diagnosed after approximately 1–5 years of Tecfidera treatment;
- previous immunosuppressive or immunomodulatory treatment;
- marked reductions in CD4+ and CD8+ T cell counts.

Magnetic resonance imaging (MRI) may be considered as part of increased vigilance for patients considered at increased risk of PML in accordance with local recommendations.

Physicians should continue to re-assess the balance of benefits and risks of Tecfidera treatment in patients with sustained moderate lymphopenia (defined as lymphocyte counts between $0.5x10^9$ per L and $0.8x10^9$ per L) for longer than 6 months. Patients who have recently stopped natalizumab (Tysabri) may develop PML in the absence of lymphopenia. Healthcare professionals should continue to monitor patients on dimethyl fumarate for any signs of neurological dysfunction. In any patient developing signs or symptoms suggestive of PML, dimethyl fumarate treatment should be stopped immediately and appropriate investigations conducted, including testing for John Cunningham virus (JCV) DNA in the cerebrospinal fluid using a quantitative polymerase chain reaction assay.

Advice for healthcare professionals:

- A small number of patients receiving dimethyl fumarate (Tecfidera) for the treatment of multiple sclerosis have developed PML associated with mild lymphopenia (defined as lymphocyte counts between $0.8x10^9$ per litre and the lower limit of normal [per local laboratory]); until now, other reported cases of PML were reported in patients with moderate to severe lymphopenia.
- Tecfidera is contraindicated in patients with suspected or confirmed PML.
- Before starting treatment:
  - do not start treatment in patients with severe lymphopenia (lymphocyte count of less than $0.5x10^9$ per litre);
  - investigate patients with low lymphocyte counts for underlying causes of this before initiation.
- During treatment:
  - all patients should have a lymphocyte count at least every 3 months;
  - conduct enhanced vigilance with close monitoring of lymphocyte counts and neurological symptoms in patients with lymphopenia and consider additional factors that may increase the risk of PML;
  - revaluate treatment in patients who have sustained moderate reductions of absolute lymphocyte counts (between $0.5x10^9$ per litre and $0.8x10^9$ per litre) for longer than 6 months; stop treatment in patients who have prolonged severe lymphopenia for longer than 6 months;
  - Tecfidera must be permanently discontinued in any patient developing PML.

In Hong Kong, Tecfidera Gastro-Resistant Capsules 240mg (HK-64410) and Tecfidera Gastro-Resistant Capsules 120mg (HK-64411) are registered pharmaceutical products containing dimethyl fumarate. Both products are registered by Eisai (Hong Kong) Co Ltd, and are prescription-only medicines. As on 5 February 2021, the DH has not received any case of ADR related to dimethyl fumarate.

Related news on the risk of progressive multifocal leukoencephalopathy associated with the use of dimethyl fumarate was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 78. The DH issued a letter to inform local healthcare professionals to draw their attention on 19 April 2016.

The current package insert of the above registered products in Hong Kong include safety information on progressive multifocal leukoencephalopathy.

Related news on cases of progressive multifocal leukoencephalopathy in patients with mild lymphopenia and updated recommendations to help minimise the risk was previously issued by the TFDA, and was reported in the Drug News Issue No. 134. The DH issued a letter to inform local healthcare professionals to draw their attention on 31 December 2020. In light of the above MHRA's announcement, the matter will be discussed by the Registration Committee.

US: FDA updates vinca alkaloid labeling for preparation in intravenous infusion bags only

On 15 January 2021, the United States (US) Food and Drug Administration (FDA) alerted healthcare professionals to labeling updates for the preparation of vinca alkaloids, a group of chemotherapy agents that includes vincristine sulfate injection, vinblastine sulfate (for) injection, and vinorelbine tartrate injection. To reduce the potential for unintended intrathecal (spinal) administration, which causes death or severe neurological injury, The FDA is working with drug application holders to remove instructions for preparation of these drugs by syringe and to recommend preparation in intravenous infusion bags only.

In 2007, the World Health Organization issued an alert about medication errors related to accidental intrathecal injection of vinca alkaloids. The Institute for Safe Medication Practices has published multiple reports about these wrong route-of-administration medication errors that resulted in adverse outcomes. In response, the FDA has twice strengthened safety warnings in labeling for vinca alkaloids to warn against intrathecal administration and emphasize the products are for intravenous administration only. As published data suggests that dispensing vinca alkaloids prepared in intravenous bags reduces the risk of medication errors due to erroneous intrathecal administration, the FDA is taking action to remove instructions for preparing vinca alkaloids in a syringe from the prescribing information for vinca alkaloids. The updated prescribing information for vinca alkaloids will only contain instructions for healthcare professionals to prepare these drugs in intravenous infusion bags.

On 24 January 2020, the FDA approved labeling changes for the brand name Navelbine (vinorelbine tartrate injection) that removed instructions for preparing it in a syringe, and drug companies are required to update generic vinorelbine product labeling to match the brand name labeling. Vinorelbine tartrate injection is indicated to treat patients with metastatic non-small cell lung cancer (NSCLC) and, in combination with cisplatin, for patients with locally advanced or metastatic NSCLC.

On 14 January 2021, the FDA removed instructions for preparing vincristine sulfate injection in a syringe. Vincristine sulfate injection is indicated to treat acute lymphocytic leukemia in children and adults, and as part of combination chemotherapy for patients with Hodgkin's disease, non-Hodgkin's malignant lymphomas (including Burkitt's lymphoma), rhabdomyosarcoma, neuroblastoma, and Wilms' tumor.

The FDA also requested more extensive labeling changes for the preparation of vinblastine sulfate (for) injection products. These labeling changes will remove instructions for preparation in a syringe and add instructions for preparation in an intravenous infusion bag. The changes should be completed during 2021.

Vinblastine sulfate injection is indicated to treat numerous malignancies including: generalized Hodgkin's disease (Stages III and IV), lymphocytic lymphoma, histiocytic lymphoma, mycosis fungoides (advanced stages), and advanced testicular carcinoma.

In Hong Kong, there are 4 registered pharmaceutical products containing vincristine sulfate, 2 registered pharmaceutical products containing vinblastine sulfate, and 7 registered pharmaceutical products containing vinorelbine tartrate for parenteral use. All products are prescription-only medicines. As on 5 February 2021, the DH has received 62 cases of ADR related to vincristine, 2 cases of ADR related to vinblastine, and 3 cases of ADR related to vinorelbine, but these cases are not related to medication errors in relation to accidental intrathecal injection. In light of the above US FDA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 18 January 2021, and the DH will remain vigilant on safety update of the drugs issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

Canada: Sofosbuvir-containing products: Assessing the potential risk of severe cutaneous adverse reactions

On 27 January 2021, Health Canada announced that it reviewed the potential risk of severe cutaneous adverse reactions (SCAR) in patients treated with sofosbuvir-containing products. The safety review was initiated when Health Canada became aware that the EMA updated the product safety information for all sofosbuvir-containing products with new information on the risk of Stevens-Johnson syndrome (SJS). The purpose of this review was to determine whether similar

actions were required in Canada.

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

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

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

In Hong Kong, there are 4 registered pharmaceutical products containing sofosbuvir, namely Sovaldi Tablets 400mg (HK-63501), Harvoni Tablets (HK-63886), Epclusa Tablets 400mg/100mg (HK-65046) and Vosevi Tablets (HK-65775). All products are registered by Gilead Sciences Hong Kong Limited, and are prescription-only medicines. As on 5 February 2021, the DH has received 16 cases of ADR related to sofosbuvir, but these cases are not related to Stevens-Johnson syndrome. In light of the above Health Canada's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 28 January 2021, and the matter will be discussed by the Registration Committee.

EU: First COVID-19 vaccine safety update published

On 29 January 2021, the EMA announced that it has released its first safety update on a coronavirus disease 2019 (COVID-19) vaccine — Comirnaty (Marketing Authorization Holder: BioNTech Manufacturing GmbH). It concludes that safety data collected on Comirnaty use in vaccination campaigns is consistent with the known safety profile of the vaccine, and no new side effects were identified.

Comirnaty is a vaccine for preventing COVID-19 in people aged 16 years and older. It contains a molecule called messenger RNA (mRNA) with instructions for producing a protein from SARS-CoV-2, the virus that causes COVID-19. The vaccine works by preparing the body to attack the spike protein on the surface of SARS-CoV-2.

The safety update includes the assessment of severe allergic reaction (anaphylaxis), which is a known side effect of the vaccine and it did not identify new aspects regarding the nature of this side effect. The Pharmacovigilance Risk Assessment Committee (PRAC) noted that a recent analysis in the US estimated the frequency of anaphylaxis as approximately 11 cases per million doses of Comirnaty administered. A frequency estimate appropriate for the EU product information could not yet be determined. The PRAC requested the marketing authorisation holder to continue reviewing all anaphylaxis cases for further assessment by the committee.

Given concerns which arose from Norway about deaths reported in frail elderly individuals after vaccination with Comirnaty, the PRAC reviewed the current reports of suspected side effects with

Safety Update

fatal outcome in individuals of any age. This review did not suggest a safety concern. In many cases concerning individuals above 65 years of age, progression of (multiple) pre-existing diseases seemed to be a plausible explanation for death. In some individuals, palliative care had already been initiated before vaccination. Before Comirnaty was granted a marketing authorisation in the EU, the safety of the vaccine was carefully assessed through large clinical trials across age groups including study participants that were 75 years of age and older. The PRAC concluded that the data did not show a link to vaccination with Comirnaty and the cases do not raise a safety concern. Based on the current data there was no need to amend the product information regarding how Comirnaty should be used, including in frail elderly individuals. Further reports will continue to be carefully monitored.

The safety and effectiveness of Comirnaty will continue to be monitored as it is used across the Member States of the EU and globally, through the EU pharmacovigilance system, additional studies by the company and independent studies coordinated by European authorities. These measures will allow regulators to swiftly assess data emerging from a range of different sources and take appropriate regulatory action to protect public health, if needed.

In Hong Kong, the above product is not a registered pharmaceutical product under the Pharmacy and Poisons Ordinance (Cap. 138) but is authorized for emergency use in Hong Kong in accordance with the Prevention and Control of Disease (Use of Vaccines) Regulation (Cap. 599K). The DH will keep vigilant on safety updates from other overseas drug regulatory authorities.

Drug Recall

DH endorsed recall of Eye-Ruby L Eye Drops (HK-34761)

On 21 January 2021, the DH endorsed a licensed drug wholesaler, Eng An Trading Company Limited (Eng An), to recall all batches of Eye-Ruby L Eye Drops (HK-34761) from the market because the product's label does not match with the registered one.

In the course of routine market surveillance by the DH, it was found that the label of the above product was different from the registered label, which rendered the product unregistered. Since the supply of unregistered pharmaceutical product contravenes the Pharmacy and Poisons Regulations (Cap. 138A), Eng An voluntarily recalls the product from the market.

The above product, containing chlorpheniramine maleate and lysozyme chloride, is an over-the-counter eye drops used for treatment of general eye discomforts. According to Eng An, the product has been supplied to local trading companies, pharmacies and medicine stores.

As on 5 February 2021, the DH has not received any ADR report related to the affected product. A notice was posted the Drug Office website on 21 January 2021 to alert the public of the product recall.

Drug Incident

DH urges public not to buy or consume product with undeclared controlled ingredients dexamethasone and piroxicam

On 28 January 2021, the DH appealed to the public not to buy or consume a product named Herbulgari as it was found to contain undeclared controlled drug ingredients.

Acting upon intelligence, samples of the above product were purchased earlier via an Internet website for analysis. The test results from the Government Laboratory revealed that the samples contained dexamethasone and piroxicam, which are Part 1 poisons under the Pharmacy and Poisons Ordinance (Cap. 138).

A joint operation with the Police was conducted on the night of 27 January 2021. During the operation, a 49-year-old man was arrested by the Police for suspected illegal sale of Part 1 poisons and an unregistered pharmaceutical product.

Dexamethasone is a steroid drug used for treating inflammation. Its side effects include moon face, high blood pressure, high blood sugar, muscle atrophy, adrenal insufficiency and osteoporosis. Piroxicam is a non-steroidal anti-inflammatory

drug used for pain relief in musculoskeletal conditions, and its side effects include gastrointestinal discomfort, gastrointestinal disorders, nausea and skin reactions. Dexamethasone and piroxicam are prescription medicines which should only be used under the advice of a medical doctor and can only be supplied at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription.

A notice was posted on the Drug Office website on 28 January 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.

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: ***Undesirable Medical Advertisements and Adverse Drug Reaction Unit,***
Drug Office, Department of Health,
Suites 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.