Drug News
藥 物 情 報

Issue Number 111

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in January 2019 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: Sulfamethoxazole containing products - Assessing the potential risk of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

On 7 January 2019, Health Canada announced that it reviewed the potential risk of DRESS with sulfamethoxazole containing products. The review was triggered because Health Canada got information from a World Health Organization (WHO) international database that suggested DRESS was being reported at a higher rate than expected for a group of drugs called sulfonamides to which sulfamethoxazole belongs.

DRESS is a severe reaction to the use of a drug that affects one or more organs, including the skin. It includes rare but serious and potentially life-threatening side effects to medications, such as fever and severe skin rash with swollen face or peeling of the skin over large areas of the body. Abnormal changes in blood cells or organ function such as the liver and kidney may also occur. These reactions usually happen 2 weeks to 2 months after starting a medication.

At the time of the review, Health Canada received 4 unique Canadian reports of DRESS that could be related to sulfamethoxazole use. Health Canada found a possible link between DRESS and sulfamethoxazole in 2 reports. The remaining 2 reports did not provide enough information to assess the role of sulfamethoxazole in the development of DRESS. This safety review also looked at 5 international reports of DRESS that could be related to sulfamethoxazole use. Only 2 of the 5 international reports met the definition of DRESS and included enough information for further review to determine if sulfamethoxazole use was the cause of DRESS. Both of these reports showed a possible link between DRESS and sulfamethoxazole use. Although the trigger for this review was information from a WHO international database that suggested the group of drugs (sulfonamides) had a higher than expected reporting rate for DRESS, the review did not find higher than expected reporting rates specifically with sulfamethoxazole. Health Canada also looked at additional information available from published literature and found 15 international reports and 4 studies of DRESS. The published reports did not use consistent criteria for making the diagnosis of DRESS. Almost half of the international reports (7/15) involved other medications or medical conditions that could have contributed to the development of DRESS. The 4 studies did not provide enough evidence to support sulfamethoxazole as the cause of DRESS.

The Canadian product safety information for sulfamethoxazole-containing products includes all other types of severe skin reactions: Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme. Although DRESS is not included in the Canadian product safety information, the Warnings and Precautions section includes some signs and symptoms of DRESS, such as severe liver damage (fulminant liver necrosis), hypersensitivity of the respiratory tract (cough, shortness of breath, and lung infiltrates), and an increase in the number of a specific type of white blood cell (eosinophilia). Additionally, impaired kidney function sometimes reported as kidney (renal) failure is included under Adverse Reactions. Health Canada also looked at additional

information available from international product safety information. International product safety information includes DRESS only for some sulfamethoxazole containing products in the European Union (EU) and Australia whose product information has been updated after 2016.

Health Canada's review of the available information concluded that there is not enough evidence at this time to establish a link between the risk of DRESS and the use of sulfamethoxazole containing products. Additionally, some of the signs and symptoms of DRESS are already included in the Canadian product safety information. For these reasons, Health Canada's review concluded that the safety information for these products is appropriate at this time.

In Hong Kong, there are 21 registered pharmaceutical products containing sulfamethoxazole, and all products are prescription-only medicines. As of 8 February 2019, the Department of Health (DH) has received 5 cases of adverse drug reaction (ADR) related to sulfamethoxazole, of which 2 cases are related to DRESS. For pharmaceutical products containing sulfonamides registered in Hong Kong, an appropriate statement concerning the product's potential to cause serious cutaneous reactions must be included in the package insert or label. In addition, some of the signs and symptoms of DRESS, such as blood disorders, hepatic and renal adverse effects, are already documented in overseas reputable drug references such as the "Martindale: The Complete Drug Reference". The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

UK: Tapentadol: risk of seizures and reports of serotonin syndrome when co-administered with other medicines

On 9 January 2019, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) announced that tapentadol may increase seizure risk in patients taking other medicines that lower seizure threshold, for example, antidepressants and antipsychotics. Serotonin syndrome has also been reported when tapentadol is used in combination with serotoninergic antidepressants.

Tapentadol is an opioid analgesic. The risk of seizures is a recognised adverse reaction for all opioid medicines. However, a recent review of safety data for tapentadol in the EU identified the need for strengthened advice about the risk of seizures. Approximately half of the identified spontaneous reports of seizure reflected co-administration of tapentadol with at least one other drug known to lower seizure threshold. These medicines include selective serotonin-reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and antipsychotics. Tapentadol should be used with care in patients with a history of seizure disorders or epilepsy because of the increased risk of seizures. Strengthened warnings on seizure risk have been added to the Summary of Product Characteristics and Patient Information Leaflets.

The MHRA is also aware of reports of serotonin syndrome identified when tapentadol is co-administered with antidepressants, such as SSRIs, SNRIs, tricyclic antidepressants and antipsychotics. Serotonin syndrome is likely when one of the following is observed: spontaneous clonus; inducible or ocular clonus with agitation or diaphoresis (sweating); tremor and hyper-reflexia; hypertonia and body temperature higher than 38°C and inducible ocular clonus. Withdrawal of the serotoninergic medicine together with supportive symptomatic care, usually brings about a rapid improvement. The continued use of tapentadol must be evaluated on an ongoing basis. Withdrawal symptoms can occur with abrupt cessation of treatment.

Healthcare professionals are advised:

- As for all opioid medicines, tapentadol can induce seizures.
- Tapentadol should be prescribed with care in patients with a history of seizure disorders or epilepsy.
- Tapentadol may increase seizure risk in patients taking other medicines that lower seizure threshold, for example, antidepressants such as SSRIs, SNRIs, tricyclic antidepressants, and antipsychotics.
- Serotonin syndrome has been reported when tapentadol is used in combination with serotoninergic antidepressants.

- Withdrawal of the serotoninergic medicine, together with supportive symptomatic care, usually brings about a rapid improvement in serotonin syndrome.

In Hong Kong, there are 8 registered pharmaceutical products containing tapentadol, and all products are prescription-only medicines. As of 8 February 2019, the DH has not received any case of ADR related to tapentadol. In light of the above MHRA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 10 January 2019 and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board (the Registration Committee).

UK: Ipilimumab: reports of cytomegalovirus (CMV) gastrointestinal infection or reactivation

On 9 January 2019, the MHRA announced that there have been post-marketing cases of gastrointestinal CMV infection or reactivation in ipilimumab-treated patients reported to have corticosteroid-refractory immune-related colitis, including fatal cases. Patients on ipilimumab who present with diarrhoea or other symptoms of colitis, and those who do not respond to steroid treatment for immune-related colitis, should be investigated to exclude other causes, including infections such as CMV.

A European review of spontaneous reports received up to 14 May 2018 identified a total of 40 cases worldwide suggestive of gastrointestinal-associated CMV infection or reactivation with ipilimumab monotherapy (29 cases) or ipilimumab in combination with nivolumab (11 cases). All cases of CMV gastrointestinal infection or reactivation occurred in patients with colitis that was refractory to corticosteroid treatment. It was not possible to determine whether these patients had immune-related colitis and then developed CMV infection or reactivation due to immunosuppressant therapy, or whether CMV infection or reactivation had been initially misdiagnosed as immune-related colitis. In 30 of the 40 patients, CMV infection/reactivation was confirmed by laboratory diagnostics, including biopsy, viral load, CMV polymerase chain reaction (PCR), CMV antigenaemia, immunoglobulin G (IgG), and immunoglobulin M (IgM) measurement. Of the 40 cases, 27 cases were on treatment with ipilimumab for malignant melanoma. The gender breakdown (where specified) was 23 men and 13 women with a median age of 67 years (range 37–87 years). The time to onset from first dose of ipilimumab ranged from 18 days to 815 days (median 92 days). Three patients died due to CMV-related colitis that was undiagnosed and then unsuccessfully treated with corticosteroids. Ten patients recovered (1 patient had sequelae), 8 patients had not recovered at the time of reporting, and 3 patients were recovering at the time of reporting.

Diarrhoea is a very common ADR associated with ipilimumab. In clinical trials of ipilimumab 3 mg/kg monotherapy, diarrhoea and colitis of any severity were reported in 27% and 8% of patients, respectively. The frequency of severe (grade 3 or 4) diarrhoea or colitis was 5% each. The median time to onset of severe or fatal (grade 3–5) immune-related gastrointestinal reactions was 8 weeks (range 5–13 weeks) from the start of treatment. Gastrointestinal reactions can also occur when ipilimumab is used in combination with nivolumab. Management recommendations for diarrhoea or colitis are provided in the Summary of Product Characteristics and are based on severity of symptoms. Diarrhoea or colitis occurring after initiation of ipilimumab must be promptly evaluated to exclude infectious or other alternate causes. For severe (Grade 3 or 4) diarrhoea and immune-related colitis, ipilimumab should be permanently discontinued and systemic high-dose intravenous corticosteroid therapy initiated.

Healthcare professionals are advised:

- Colitis occurs commonly in patients treated with ipilimumab for advanced melanoma; advise patients to contact their healthcare professional immediately at the onset of symptoms of colitis (including diarrhoea, blood in stools, or abdominal pain).
- If patients on ipilimumab present with diarrhoea or colitis, investigate possible causes, including infections; perform a stool infection work-up and screen for CMV.
- For patients with immune-related colitis that is corticosteroid refractory, use of an

additional immunosuppressive agent should only be considered if other causes are excluded (including with screening for CMV, culture, *Clostridium difficile*, ova, and parasite) using viral PCR on biopsy, and other viral, bacterial, and parasitic causes.

In Hong Kong, there are 2 registered pharmaceutical products containing ipilimumab, and both products are prescription-only medicines. As of 8 February 2019, the DH has received 11 cases of ADR related to ipilimumab, but these cases are not related to gastrointestinal CMV infection or reactivation. In light of the above MHRA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 10 January 2019 and the matter will be discussed by the Registration Committee.

Canada: Health Canada safety review finds possible link between Fibristal and risk of liver injury

On 11 January 2019, Health Canada informed Canadians that its safety review of Fibristal (ulipristal acetate) found a possible link between its use and the risk of a rare but serious liver injury.

Fibristal is approved in Canada to treat signs and symptoms of a type of non-cancerous tumour in the uterus (fibroids) in women of childbearing age.

Health Canada initiated its safety review after receiving four international reports of liver injury leading to liver transplants.

To support the safe use of this medication, Health Canada has worked with the manufacturer to update the Canadian product safety information for Fibristal.

The product safety information updates include new restrictions for use. In particular, Fibristal should not be used in women who currently have, or have previously had liver problems. Intermittent use (more than one treatment course) should be restricted to women of childbearing age who are not eligible for surgery to remove their fibroids. In addition, the product safety information has been updated to include requirements for liver function monitoring before, during and after treatment.

Health Canada will continue to monitor the use of Fibristal and will take action if new safety risks are identified.

In Hong Kong, Esmya (ulipristal acetate) Tablets 5mg (HK-62553) is a pharmaceutical product registered by Orient Europharma Co. Ltd, and is a prescription-only medicine. As of 8 February 2019, the DH has not received any case of ADR related to Esmya. Related news was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 98, 100, 103 and 106. The DH issued a letter to inform local healthcare professionals to draw their attention on the risk of serious liver injury on 12 February 2018. The safety updates issued by overseas drug regulatory authorities has been discussed by the Registration Committee on 12 December 2018 and decided that the relevant warnings should be included in the package insert of the product.

US: Prinston Pharmaceutical Inc. issues voluntary nationwide recall of Irbesartan and Irbesartan HCTZ Tablets due to detection of a trace amount of unexpected impurity, *N*- nitrosodiethylamine (NDEA) in the products

On 18 January 2019, the United States (US) Food and Drug Administration (FDA) announced that Prinston Pharmaceutical Inc., dba Solco Healthcare LLC., has initiated a voluntary recall of one lot of Irbesartan and seven lots of Irbesartan HCTZ Tablets to the consumer level due to the detection of trace amount of an unexpected impurity found in an active pharmaceutical ingredient (API) manufactured by Zhejiang Huahai Pharmaceuticals.

Prinston is only recalling lots of Irbesartan-containing products that contain NDEA above the acceptable daily intake levels released by the FDA. The product subject to recall are listed below and packaged in bottles.

Product	NDC Code	Lot Number	Expiry Date
IRBESARTAN TABLETS 300MG 90CT	43547-376-09	331B18009	02/2021
IRBESARTAN/ HCTZ 300MG/12.5MG 30CT TABLETS	43547-331-03	327A18001, 327A18002	03/2021
IRBESARTAN/ HCTZ 300MG/12.5MG 90CT TABLETS	43547-331-09	327B18008, 327B18009	03/2021
IRBESARTAN/ HCTZ 150MG/12.5MG 30CT TABLETS	43547-330-03	325D18004, 325D18005	03/2021
IRBESARTAN/ HCTZ 150MG/12.5MG 90CT TABLETS	43547-330-09	325B18004	03/2021

NDEA is a substance that occurs naturally in certain foods, drinking water, air pollution, and industrial processes and has been classified as a probable human carcinogen as per International Agency for Research on Cancer (IARC) classification.

As of 18 January 2019, Prinston Pharmaceutical Inc. has not received any reports of adverse events related to this recall.

In Hong Kong, as of 8 February 2019, there are 251 registered pharmaceutical products containing valsartan (83 products), candesartan (19 products), irbesartan (63 products), losartan (69 products) and olmesartan (17 products). All products are prescription-only medicines.

Regarding impurities in valsartan, a public announcement was issued on 6 July 2018, and the DH issued letters to inform local healthcare professionals on 6 July 2018, 9 July 2018, 25 July 2018 and 3 August 2018. Related news for the detection of impurities in sartan-containing products was also previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 105, 106, 107, 108, 109 and 110.

In brief, there are four manufacturers, namely Zhejiang Huahai, Zhejiang Tianyu and Zhuhai Rundu in China and Hetero Labs Limited in India, reported to have detection of trace amounts of *N*-nitrosodimethylamine (NDMA) in the valsartan API by various overseas drug regulatory authorities. The DH contacted the certificate holders of all registered valsartan products to follow up on the local impact regarding valsartan API produced by the above mentioned manufacturers.

For API produced by Zhejiang Huahai, there are 5 affected products (HK-61786, HK-61787, HK-61784, HK-61785 and HK-60794) marketed in Hong Kong. The DH instructed the certificate holders to recall all the products from the market as a precautionary measure on 6 July 2018, and the DH noted that all the recalls have been completed.

For API produced by Zhejiang Tianyu, amongst the registered pharmaceutical products containing valsartan, there is only one product namely Retoni Tablets 80mg (HK-65604) registered by Swiss Pharmaceutical Co Limited (Swiss Pharmaceutical) which has used API produced by Zhejiang Tianyu and is available in the local market. As confirmed with Swiss Pharmaceutical, the API was tested by the Taiwan Food and Drug Administration (TFDA) and the company has not received any notice from the TFDA for NDMA contamination. The DH collected samples of Retoni tablets for analysis and no NDMA was detected.

For API produced by Zhuhai Rundu and Hetero Labs Limited, the certificate holders confirmed that the valsartan products available in local market are not manufactured using API produced by Zhuhai Rundu or Hetero Labs Limited.

Regarding the announcements issued by various overseas drug regulatory authorities on the detection of the second impurity of NDEA in the valsartan API produced by Zhejiang Huahai, there should be no local impact as all valsartan products manufactured using API produced by Zhejiang Huahai have been recalled from the market.

Regarding the announcements issued by various overseas drug regulatory authorities on the detection of NDEA in the valsartan API produced by Mylan Laboratories Limited in India, the

certificate holders confirmed that the valsartan products available in local market are not manufactured using API produced by this company.

Regarding the European Medicines Agency's (EMA) and the US FDA's announcement on the detection of NDEA in the losartan API produced by Hetero Labs Limited, the US FDA's announcement on NDEA in the losartan API produced by Zhejiang Huahai, the TFDA's announcement on NDEA in the losartan API produced by IPCA in India, the announcements issued by the EMA, US FDA and TFDA on NDEA in the irbesartan API produced by Aurobindo Pharma in India, and the above US FDA's announcement on the detection of NDEA in the irbesartan API produced by Zhejiang Huahai, the DH has contacted the certificate holders of all registered candesartan, irbesartan, losartan and olmesartan products and will continue to follow up on the impact of NDEA impurities on the products available in the local market. On 20 December 2018, the DH endorsed Actavis Hong Kong Limited to recall one batch (batch number: 058818) of Irbesartan HCT Actavis Tablets 150/12.5mg (HK-63378) from the market as a precautionary measure because an impurity was detected in one of the raw materials of this batch of product, a public announcement was issued on 20 December 2018. The DH is closely monitoring the recall.

As of 8 February 2019, the DH has received 16 cases of ADR related to valsartan, candesartan, irbesartan, losartan and olmesartan. None of them is concluded to be related to the presence of NDMA and/or NDEA. The DH will keep vigilant on any further updates on the matter issued by overseas regulatory authorities.

Patients who are taking the above products should not stop taking the medicines, but should seek advice from their healthcare professionals as soon as possible for proper arrangement.

The DH has provided update information at Drug Office's website (www.drugoffice.gov.hk) and will remain vigilant on any safety update related to the impurities NDMA and NDEA in sartan-containing (candesartan, irbesartan, losartan, olmesartan and valsartan) products.

EU: No new patients should start treatment with Lartruvo after study shows cancer medicine does not prolong life

On 23 January 2019, the EMA of the EU announced that preliminary results from the ANNOUNCE study show that Lartruvo (olaratumab) in combination with doxorubicin is not more effective at prolonging the lives of patients with soft tissue cancer than doxorubicin alone.

While full results from the study are awaited, the EMA is recommending that no new patients should start treatment with the medicine. For patients currently being treated with Lartruvo, their doctor may consider continuing treatment with the medicine if they appear to benefit from it. It is estimated that around 1,000 patients are currently treated with Lartruvo in the EU. Based on the information available so far, there are no new safety concerns with the medicine, with side effects reported with the combination being similar to those with doxorubicin alone.

At time of its approval, data on the effects of Lartruvo were limited because of the small number of patients included in the main study which supported authorisation. The medicine was therefore granted a marketing authorisation on condition that the company provides additional data from the ANNOUNCE study in order to confirm the efficacy and safety of the medicine.

Healthcare professionals will be informed in writing of the preliminary results of the study and the current treatment recommendations. The EMA will communicate further as appropriate.

Information for healthcare professionals:

- The phase 3 study ANNOUNCE evaluated Lartruvo in combination with doxorubicin in patients with advanced or metastatic soft tissue sarcoma and did not confirm the clinical benefit of Lartruvo in combination with doxorubicin as compared with doxorubicin alone.
- The study did not meet its primary objective to prolong survival in the overall population (hazard ratio [HR]: 1.05; median 20.4 vs. 19.7 months for Lartruvo plus doxorubicin

and doxorubicin, respectively) or in the leiomyosarcoma sub-population (HR: 0.95; median 21.6 months for Lartruvo plus doxorubicin versus 21.9 months for doxorubicin).
- Additionally, no benefit was shown in terms of prolonging progression-free survival in the overall population (HR: 1.23; median 5.4 months for Lartruvo plus doxorubicin versus 6.8 months for doxorubicin), which was one of the secondary objectives of the study.
- As a consequence, no new patients should be prescribed Lartruvo.
- While further assessment of the study results is ongoing, doctors may consider continuing Lartruvo treatment in patients who experience clinical benefit.
- No new safety concerns were identified during the study and the safety profile was comparable in the two treatment arms.
- A letter will be sent to all healthcare professionals expected to prescribe the medicine to inform them of the preliminary results of the study and the current treatment recommendations.

In Hong Kong, there are 2 registered pharmaceutical products containing olaratumab, namely Lartruvo Concentrate for Solution for Infusion 500mg/50ml (HK-66024) and Lartruvo Concentrate for Solution for Infusion 190mg/19ml (HK-66025). Both products are registered by Eli Lilly Asia, Inc., and are prescription-only medicines. As of 8 February 2019, the DH has not received any case of ADR related to olaratumab. In light of the above EMA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 24 January 2019. As further assessment of the study results is ongoing, the DH will remain vigilant on safety update of the drug issued by the EMA and other overseas drug regulatory authorities for consideration of any action deemed necessary.

Canada: Hydrochlorothiazide - Assessing the potential risk of non-melanoma skin cancer (NMSC)

On 30 January 2019, Health Canada announced that it reviewed the potential risk of NMSC with hydrochlorothiazide use. The safety review was triggered by the publication of two recent studies suggesting a higher risk of NMSC with prolonged use (three years or more) of hydrochlorothiazide. NMSC is the most commonly diagnosed cancer in Canada. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the two major types of NMSC.

Health Canada reviewed the relevant studies on the topic. Data from studies were combined to estimate the overall risk of NMSC with the use of hydrochlorothiazide. The level of the certainty for the findings was also assessed. Five studies analyzing data from thousands of patients investigated the risk of NMSC with the use of hydrochlorothiazide alone or in combination with other drugs. All relevant studies were from North America and Europe, with a majority of patients of light-coloured skin. Studies had important limitations in their designs and methods. Health Canada's review found that the risks for SCC and BCC increase with prolonged use (three years or more) of hydrochlorothiazide. After several years of use, the risk could be up to 4 times higher for SCC and 1.25 times higher for BCC compared to the risk in patients not treated with hydrochlorothiazide. Although substantial uncertainty exists regarding these findings, risk estimates reflect the current best evidence addressing the topic. NMSC is therefore considered a potential risk of prolonged hydrochlorothiazide treatment.

Health Canada's review of the relevant evidence suggests that there might be a risk of NMSC with prolonged use of hydrochlorothiazide. Given the substantial uncertainty for the findings, NMSC should be considered a potential risk of prolonged hydrochlorothiazide treatment. Patients taking hydrochlorothiazide should be informed of the potential risk of NMSC and advised to regularly check their skin for new marks or growths as well as changes to existing ones. Patients should report any suspicious skin marks or growths to their healthcare professional. Patients should be advised to limit exposure to sunlight, avoid the use of tanning equipment, and use adequate sun protection (e.g., sun protection factor (SPF) 30 or higher, clothing, and a hat) to minimize the risk of skin cancer. Alternatives to hydrochlorothiazide may be

Safety Update

considered for patients who are at a particularly high risk for NMSC (e.g., light-coloured skin, known personal or family history of skin cancer, ongoing immunosuppressive therapy, etc.).

Health Canada will notify the manufacturers to update the product safety information of all hydrochlorothiazide-containing products to inform about this potential risk and the preventive measures to consider when taking hydrochlorothiazide.

In Hong Kong, there are 104 registered pharmaceutical products containing hydrochlorothiazide, and all products are prescription-only medicines. As of 8 February 2019, the DH has received 2 cases of ADR related to hydrochlorothiazide, but these cases are not related to skin cancer. Related news was previously issued by the MHRA and Singapore Health Sciences Authority, and was reported in the Drug News Issue No. 109. The DH issued a letter to inform local healthcare professionals to draw their attention on 15 November 2018. As previously reported, the matter will be discussed by the Registration Committee.

Drug Recall

DH endorsed batch recall of Entocort Controlled Ileal Release 3mg Capsule (HK-42387)

On 4 January 2019, the DH endorsed a licensed drug wholesaler, Associated Medical Supplies Companies Ltd (Associated), to recall one batch (batch number: 60032034) of Entocort Controlled Ileal Release 3mg Capsule (HK-42387) from the market because the outer box label of the product does not match with the registered particulars.

The DH was notified by Associated on 4 January 2019 that the outer box of the Entocort Controlled Ileal Release 3mg Capsule with new label has been used. However, such change in the label has not been approved by the Pharmacy and Poisons Board and renders the product unregistered. Since the supply of unregistered pharmaceutical products contravenes the Pharmacy and Poisons Regulations (Cap. 138A), Associated voluntarily recalled the above affected batch from the market.

The above product contains budesonide is a prescription medicine used for the treatment of Crohn's disease affecting the ileum and ascending colon. According to Associated, 92 boxes have been supplied to Hospital Authority and a local private doctor.

As of 8 February 2019, the DH has not received any case of ADR in connection with the products concerned. A notice was posted on the Drug Office website on 4 January 2019 to alert the public of the product recall.

DH endorsed batch recall of Cidofovir (Heritage) 375mg/5ml Injection

On 16 January 2019, the DH endorsed a licensed drug wholesaler, Link Healthcare Hong Kong Limited (Link), to recall one batch of Cidofovir (Heritage) 375mg/5ml Injection (batch number: VCIA084) from the market because of a potential quality issue.

The DH received notification from Link that the manufacturer of the product in India advised Link to recall one batch of product from the market due to a potential lack of container integrity for the product. Link recalled the affected batch as a precautionary measure.

The above product, containing Cidofovir, is not a registered pharmaceutical product in Hong Kong but was imported for the treatment of particular patients by a registered medical practitioner. According to Link, 5 bottles of the affected batch have been supplied to one private hospital.

A notice was posted on the Drug Office website on 16 January 2019 to alert the public of the product recall.

Drug Recall

DH endorsed batch recall of Adrenalin Chloride 1:1000 30mg/30ml Injection

On 25 January 2019, the DH endorsed a licensed drug wholesaler, Trackcircle.com Limited (Trackcircle), to recall one batch of Adrenalin Chloride Injection 1:1000 30mg/30ml (batch number: F7J025) from the market because of a potential quality issue.

The DH received notification from Trackcircle that the manufacturer of the product in Italy is recalling one batch (batch number: F7J025) of the product because the samples failed the assay test during the ongoing stability study. Trackcircle recalls the affected batch as a precautionary measure.

The above product, containing adrenaline chloride, is not a registered pharmaceutical product in Hong Kong but was imported for the treatment of particular patients by registered medical practitioners. According to Trackcircle, 2,290 bottles of the affected batch have been supplied to Hospital Authority. A notice was posted on the Drug Office website on 25 January 2019 to alert the public of the product recall.

Drug Incident

DH urged not to buy or use facial mask with controlled substance fluocinolone acetonide

On 14 January 2019, the DH appealed to the public not to buy or use a facial mask named MYRTUS 8 MASK, which was found to contain an undeclared and controlled substance.

Acting upon a public enquiry, the DH found that the above facial mask has been offered for sale at two retail shops in Causeway Bay. Samples of the product were collected from the two shops for analysis. The Government Laboratory's test results revealed that the samples contained fluocinolone acetonide, a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138).

Fluocinolone acetonide is a steroid substance. Products containing fluocinolone acetonide should only be sold at pharmacies under the supervision of registered pharmacists upon a doctor's prescription. Inappropriate or excessive application of steroids could cause skin problems and body-wide side effects like moon face, high blood pressure, high blood sugar, muscle atrophy, adrenal insufficiency and osteoporosis.

Press release was posted on the Drug Office website on 14 January 2019 to alert the public of the drug incident.

Man arrested for suspected illegal sale of unregistered pharmaceutical products

On 17 January 2019, the DH conducted an operation against the sale of unregistered pharmaceutical products, during which a 31-year-old man was arrested by the Police for suspected illegal sale of unregistered pharmaceutical products and Part 1 poisons.

Acting upon a public complaint, some pharmaceutical products for slimming and muscle pain were found offered for sale via a social media platform and the Internet. The products are labelled in Japanese and do not bear Hong Kong pharmaceutical product registration numbers.

The products for slimming are believed to contain frusemide, rosuvastatin or levothyroxine while the product for muscle pain is believed to contain felbinac. The above ingredients are all Part 1 poisons under the Pharmacy and Poisons Ordinance (Cap. 138).

Frusemide is a diuretic and its side effects include low blood pressure and electrolyte imbalance. Rosuvastatin is used for the treatment of hypercholesterolemia and its side effects include muscle pain and headache. Levothyroxine is used for the treatment of hypothyroidism and its side effects include fast and irregular heart beat and hypertension. Felbinac is a non-steroidal anti-

inflammatory drug used topically to relieve pain. Inappropriate use of felbinac may cause erythema and dermatitis.

Products containing the above ingredients should only be used upon the advice of a medical practitioner and be supplied by a pharmacy under the supervision of a registered pharmacist. Products containing frusemide, rosuvastatin or levothyroxine are also prescription medicines.

Weight control should be achieved through a balanced diet and appropriate exercise. The public should consult healthcare professionals before using any medication for weight control. The public may visit the website of the Drug Office of the DH for health messages on weight control and slimming products and information on slimming products with undeclared Western drug ingredients.

People who have purchased the above products should stop using them and consult healthcare professionals for advice if they are in doubt or feeling unwell after use. Press release was posted on the Drug Office website on 17 January 2019 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 accordnance 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: ***Pharmacovigilance Unit,***
Drug Office, Department of Health,
Rm 1856, 18/F, Wu Chung House,
213 Queen's Road East,
Wan Chai, Hong Kong

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.