Drug News
藥 物 情 報

Issue Number 143

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

The United States: FDA requires warnings about increased risk of serious heart-related events, cancer, blood clots, and death for JAK inhibitors that treat certain chronic inflammatory conditions

On 1 September 2021, the US Food and Drug Administration (FDA) announced that, based on a completed FDA review of a large randomized safety clinical trial, it has concluded there is an increased risk of serious heart-related events such as heart attack or stroke, cancer, blood clots, and death with the arthritis and ulcerative colitis medicines Xeljanz and Xeljanz XR (tofacitinib).

This trial compared Xeljanz with another type of medicine used to treat arthritis called tumor necrosis factor (TNF) blockers in patients with rheumatoid arthritis. The trial's final results also showed an increased risk of blood clots and death with the lower dose of Xeljanz. A prior Drug Safety Communication based upon earlier results from this trial, reported an increased risk of blood clots and death only seen at the higher dose.

FDA was requiring new and updated warnings for two other arthritis medicines in the same drug class as Xeljanz, called Janus kinase (JAK) inhibitors, Olumiant (baricitinib) and Rinvoq (upadacitinib). Olumiant and Rinvoq had not been studied in trials similar to the large safety clinical trial with Xeljanz, so the risks had not been adequately evaluated. However, since they share mechanisms of action with Xeljanz, FDA considered that these medicines may have similar risks as seen in the Xeljanz safety trial.

Two other JAK inhibitors, Jakafi (ruxolitinib) and Inrebic (fedratinib), are not indicated for the treatment of arthritis and other inflammatory conditions and so are not a part of the updates being required to the prescribing information for Xeljanz, Xeljanz XR, Olumiant, and Rinvoq. Jakafi and Inrebic are used to treat blood disorders and require different updates to their prescribing information. If FDA becomes aware of any additional safety information or data that warrants updates to the prescribing information for these medicines, FDA may take further action and will alert the public.

FDA was requiring revisions to the Boxed Warning, FDA's most prominent warning, for Xeljanz/Xeljanz XR, Olumiant, and Rinvoq to include information about the risks of serious heart-related events, cancer, blood clots, and death.

Health care professionals should consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Xeljanz/Xeljanz XR, Olumiant, or Rinvoq. This is particularly the case in patients who are current or past smokers, those with other cardiovascular risk factors, those who develop a malignancy, and those with a known malignancy other than a successfully treated nonmelanoma skin cancer. Reserve these medicines for patients who have had an inadequate response or intolerance to one or more TNF blockers. Counsel patients about the benefits and risks of these medicines and advise them to seek emergency medical attention if they experience signs and symptoms of a heart attack, stroke, or blood clot.

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) which are registered by Pfizer Corporation Hong Kong Limited; 2 products containing baricitinib, namely Olumiant Tablets 2mg (HK-65663) and Olumiant Tablets 4mg (HK-65664) which are

registered by Eli Lilly Asia, Inc.; and one product containing upadacitinib, namely Rinvoq Prolonged-Release Tablets 15mg (HK-66872) which is registered by Abbvie Limited. All products are prescription-only medicines.

As of the end of September 2021, the Department of Health (DH) had received 8 cases of adverse drug reaction related to tofacitinib (of which one case is lung cancer and 3 cases are deep vein thrombosis); 3 cases related to baricitinib (of which one case is deep vein thrombosis); and 4 cases related to upadacitinib.

Related news on the risk of blood clots and death of tofacitinib was previously issued by various overseas drug regulatory authorities, and was reported on Drug News Issue Nos. 112, 117, 125, 128 and 136. The DH issued letters to inform local healthcare professionals to draw their attention on 29 Jul 2019 and 19 Jun 2020. In Dec 2019, the Registration Committee of the Pharmacy and Poisons Board discussed the matter, and decided that the sales pack or package insert of tofacitinib products should include safety information about increased risk of blood clots and death with higher dose (10 mg twice daily).

Related news on the risk of blood clots of baricitinib was previously issued by various overseas drug regulatory authorities, and was reported on Drug News Issue No. 125. The DH issued letters to inform local healthcare professionals to draw their attention on 19 Jun 2020. The current local product inserts already contain safety information on the risk of venous thromboembolism.

Related news on the risk of serious heart-related problems and cancer of tofacitinib was previously issued by various overseas drug regulatory authorities, and was reported on Drug News Issues Nos. 112, 117, 125, 136, 137 and 140. The DH issued letters to inform local healthcare professionals to draw their attention on 15 Jun 2021.

In light of the above FDA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 2 September 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

European Union: COVID-19 vaccines: EMA reviewing cases of multisystem inflammatory syndrome

On 3 September 2021, the European Medicines Agency (EMA) announced that EMA's safety committee (PRAC) was assessing whether there is a risk of multisystem inflammatory syndrome (MIS) with COVID-19 vaccines following a report of MIS with Comirnaty. The case occurred in a 17-year old male in Denmark who has since fully recovered.

Some cases of MIS were also reported in the European Economic Area (EEA) following vaccination with other COVID-19 vaccines. As of 19 August 2021, cases reported as MIS in children in the EEA from the EudraVigilance database were: Comirnaty (5 cases); Spikevax (1 case); Vaxzevria (no case); COVID-19 Vaccine Janssen (1 case).

Some of the cases occurred in adults rather than in children.

MIS is a serious inflammatory condition affecting many parts of the body and symptoms can include tiredness, persistent severe fever, diarrhoea, vomiting, stomach pain, headache, chest pain and difficulty breathing. MIS has previously been reported following COVID-19 disease. The Danish patient, however, had no history of COVID-19.

MIS is rare and its incidence rate before the COVID-19 pandemic estimated from 5 European countries was around 2 to 6 cases per 100,000 per year in children and adolescents below 20 years of age and below 2 cases per 100,000 per year in adults aged 20 years or more.

At this stage, as of 3 September 2021, there was no change to the recommendations in European Union (EU) for the use of COVID-19 vaccines.

The PRAC encouraged all healthcare professionals to report any cases of MIS and other adverse events in people having these vaccines.

The PRAC would assess the available data on MIS to determine whether the condition can be caused by the vaccine and recommend whether any changes to the product information of the vaccines are needed. EMA and national authorities would provide further updates as necessary.

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). The DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

European Union: Imbruvica: new safety signal for use in combination with rituximab and ACE inhibitors

On 3 September 2021, the EMA announced that PRAC had discussed a direct healthcare professional communication (DHPC) containing important safety information for Imbruvica.

This DHPC aims to inform healthcare professionals about a new safety signal of sudden or cardiac death with Imbruvica (ibrutinib) when used in combination with rituximab and angiotensin-converting enzyme (ACE) inhibitors. The signal was recognized following a review of the findings of a clinical trial.

Imbruvica is a medicine for treating the blood cancers mantle cell lymphoma, chronic lymphocytic leukaemia (CLL) and Waldenström's macroglobulinaemia (also known as lymphoplasmacytic lymphoma).

An interim analysis of the clinical trial suggested that the risk of sudden or cardiac death in patients on an ACE inhibitor when entering the study was increased in patients randomised to ibrutinib and rituximab, compared to those randomised to fludarabine, cyclophosphamide and rituximab.

While the PRAC is reviewing the signal, as a precautionary measure, for patients with CLL currently receiving ibrutinib plus rituximab together with an ACE inhibitor, the PRAC advises healthcare professionals to reconsider the treatment strategy.

For patients with CLL on ACE-inhibitors who have not yet started treatment with ibrutinib plus rituximab, the treatment strategy should be reconsidered before commencing ibrutinib.

The PRAC would communicate final conclusions and recommendations as soon as the evaluation has been completed.

The DHPC for Imbruvica would be forwarded to EMA's human medicines committee, the CHMP. Following the CHMP decision, the DHPC would be disseminated to healthcare professionals by the marketing authorisation holder, according to an agreed communication plan, and published on EMA's website and in national registers in EU Member States.

In Hong Kong, there are 4 registered pharmaceutical products containing ibrutinib, namely Imbruvica Capsules 140mg (HK-64088), Imbruvica Capsules 140mg (HK-65397), Imbruvica Tablets 140mg (HK-67062) and Imbruvica Tablets 280mg (HK-67063). The products are registered by Johnson & Johnson (Hong Kong) Ltd., and are prescription-only medicines. As of the end of September 2021, the DH had received 16 cases of adverse drug reaction related to ibrutinib, but these cases are not related to sudden or cardiac death. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Singapore: Update to Singapore package insert of Prostin E2 Vaginal Tablet (dinoprostone)

On 8 September 2021, Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Pfizer Pte Ltd to inform healthcare professionals that the package insert of Prostin E2 Vaginal Tablet (dinoprostone) had been updated to strengthen the risk minimisation measures to manage the known risk of foetal and neonatal death associated with uterine hyperstimulation and uterine rupture.

The new safety information included a statement to restrict usage to qualified healthcare professionals and hospitals and clinics with specialised obstetric units that have facilities for continuous monitoring. Other information included warnings against exceeding the maximum recommended dose or shortening the dosing interval, advice to consider concomitant medicine as well as maternal or foetal status, and documentation of this safety issue in the package insert.

In Hong Kong, there are 2 registered pharmaceutical products containing dinoprostone which are vaginal tablets/pessaries, namely Prostin E2 Vag Tab 3mg (HK-19734) registered by Pfizer Corporation Hong Kong Limited; and Propess

Vaginal Pessaries 10mg (HK-41119) registered by Ferring Pharmaceuticals Ltd. Both products are prescription-only medicines. As of the end of September 2021, the DH had not received any case of adverse drug reaction related to dinoprostone. In light of the above HSA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 10 September 2021. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Australia: Erenumab and hypertension

On 9 September 2021, Therapeutic Goods Administration (TGA) announced that the Product Information (PI) for erenumab had been updated with a warning statement about a potential causal relationship between the drug and hypertension.

The 'Special Warnings and Precautions' section (Section 4.4) of the PI for erenumab had been updated to state that development of hypertension and worsening of pre-existing hypertension have been reported following use of the drug in the postmarketing setting internationally. Many of the affected patients had pre-existing hypertension or risk factors for hypertension. There were cases requiring pharmacological treatment and, in some cases, hospitalisation.

Hypertension can occur at any time during treatment, but it was most frequently reported within 7 days of dose administration. In the majority of cases, the onset or worsening of hypertension was reported after the first dose of erenumab. The drug was discontinued in many of the reported cases. There has been one report of hypertension associated with erenumab reported in Australia, to the TGA.

Additionally, hypertension has been added under 'Vascular disorders' in the 'Adverse Effects' section (Section 4.8) of the erenumab PI.

Health professionals are advised:

- If they are treating a patient with erenumab, they should monitor them for new-onset hypertension or worsening of pre-existing hypertension.
- If hypertension is observed and evaluation fails to establish an alternative etiology, consider whether discontinuation of erenumab is warranted.

In Hong Kong, there are 2 registered pharmaceutical products containing erenumab, namely Aimovig Solution For Injection In Pre-filled Pen 70mg/ml (HK-66406) and Aimovig Solution For Injection In Pre-filled Pen 140mg/ml (HK-66847). Both products are registered by Novartis Pharmaceuticals (HK) Limited, and are prescription-only medicines. As of the end of September 2021, the DH had received 2 cases of adverse drug reaction related to erenumab, of which one case is related to hypertension. In light of the above TGA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 10 September 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

The United Kingdom: Topical corticosteroids: information on the risk of topical steroid withdrawal reactions

On 15 September 2021, Medicines and Healthcare products Regulatory Agency (MHRA) announced that rarely, severe adverse effects can occur on stopping treatment with topical corticosteroids, often after long-term continuous or inappropriate use of moderate to high potency products.

Topical corticosteroids are safe and highly effective treatments for skin conditions such as eczema, psoriasis, and atopic dermatitis when used correctly. They are available in different potencies: mildly potent (for example, hydrocortisone); moderately potent (for example, clobetasone); potent (for example, beclometasone); and very potent (for example, clobetasol).

During its review MHRA considered data gathered from Yellow Card reports and identified 55 reports indicative of topical steroid withdrawal reactions, most of which were reported by patients. MHRA also considered information available in the literature and from other regulators. MHRA is unable to estimate the frequency of these reactions. However, given the number of patients who use topical corticosteroids, MHRA understands reports of severe withdrawal reactions to be very infrequent.

Information about the risks and characteristics of topical steroid withdrawal reactions would be added to the Summaries of Product Characteristics and the Patient Information Leaflets for topical corticosteroid medicines.

Topical steroid withdrawal reactions are thought to occur after prolonged, frequent, or inappropriate use of moderate to high potency topical corticosteroids. Topical steroid withdrawal reactions can develop after application of a topical corticosteroid at least daily for longer than a year. In children they can occur within as little as 2 months of daily use. People with atopic dermatitis are thought to be most at risk of developing topical steroid withdrawal reactions. It has been reported that the signs and symptoms occur within days to weeks after discontinuation of long-term topical corticosteroid treatment. They are most commonly seen after treatment of sensitive areas such as the face or genitals.

The most common reaction is a rebound (or flare) of the underlying skin disorder such as atopic dermatitis. However, patients have described a specific type of topical steroid withdrawal reaction in which skin redness extends beyond the initial area of treatment with burning or stinging and that is worse than the original condition. It can be difficult to distinguish a flare up of the skin disorder, which would benefit from further topical steroid treatment, and a topical steroid withdrawal reaction.

A topical steroid withdrawal reaction should be considered if:

- burning rather than itch is the main symptom
- redness is confluent rather than patchy (which may not be so obvious in people with darker skin) (redness can be a spectrum of pink, red, and purple, or subtle darkening of the existing skin colour, which can vary depending on the skin tone of the individual)
- rash resembles atopic dermatitis but involves unusual sites and is 'different' to the skin condition that the patient has experienced before
- there has been a history of continuous prolonged use of a moderate or high potency topical corticosteroid

Skin biopsy is generally unhelpful to distinguish topical steroid withdrawal reactions from a flare of the underlying skin disorder because the histopathology overlaps.

If the patient's skin condition fails to improve, before prescribing a more potent corticosteroid, consider possible diagnoses such as rosacea, peri-oral dermatitis, infection and allergy to the topical corticosteroid or other topical medications, including moisturisers or cosmetics. Patch testing may identify some cases of contact allergy. If a severe rebound of atopic dermatitis is suspected, review the guidance on alternative treatments.

Advice for healthcare professionals:

- long-term continuous or inappropriate use of topical corticosteroids, particularly those of moderate to high potency, can result in the development of rebound flares after stopping treatment; there are reports of such flares taking the form of a dermatitis with intense redness, stinging, and burning that can spread beyond the initial treatment area
- when prescribing a topical corticosteroid, consider the lowest potency needed
- advise patients on the amount of product to be applied; underuse can prolong treatment duration
- inform patients how long they should use a topical corticosteroid, especially on sensitive areas such as the face and genitals
- inform patients to return for medical advice if their skin condition worsens while using topical corticosteroid, and advise them when it would be appropriate to re-treat without a consultation
- for patients currently on long-term topical corticosteroid treatment, consider reducing potency or frequency of application (or both)
- be vigilant for the signs and symptoms of topical steroid withdrawal reactions

In Hong Kong, there are registered pharmaceutical products containing topical corticosteroids such as hydrocortisone, clobetasone and clobetasol. As of the end of September, the DH had received 5 cases of adverse drug reaction related to corticosteroids dermatological preparations, but these cases are not related to steroid withdrawal reactions. In light of the above MHRA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 16 September 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Australia: Propylthiouracil and carbimazole: use in pregnancy

On 15 September 2021, the TGA announced that the pregnancy category for both propylthiouracil and carbimazole was being changed from category C to category D. A TGA safety assessment found that the PI documents for these medicines adequately described known risks relating to

congenital abnormalities in neonates and therefore no changes or additions were required. However, it was determined that category D was the appropriate category for these products.

Reviewing a safety signal relating to congenital abnormalities for propylthiouracil and carbimazole, the TGA found that the current Australian PI documents for both medicines contained sufficient safety information under 'Section 4.6 Fertility, Pregnancy and Lactation'. Additionally, the carbimazole PI contains additional information on women of childbearing potential and pregnancy in 'Section 4.4 Special Warnings and Precautions for Use'.

However, the products were previously categorised under pregnancy category C, which is defined as 'Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible.'

As cases of congenital abnormalities have been reported in the post-market setting following use of these medicines, this category is no longer considered the correct pregnancy categorisation.

Category D is defined as 'Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human foetal malformations or irreversible damage' and reflects the post-market experience with these medicines.

Propylthiouracil and carbimazole should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

In Hong Kong, there are registered pharmaceutical products containing propylthiouracil (5 products) and carbimazole (6 products). All products are prescription-only medicines. As of the end of September 2021, the DH had not received any case of adverse drug reaction related to propylthiouracil. The DH had received one case of adverse drug reaction related to carbimazole, but this case is not related to congenital abnormalities.

Related news on the risk of congenital malformations associated with the use of carbimazole during pregnancy was previously issued by various overseas drug regulatory authorities, and was reported on Drug News Issue Nos. 112 and 119. Currently, the sales pack or package insert of locally registered carbimazole-containing products should include safety information relevant to the risk of congenital malformations. Related news on the risk of birth defects associated with the use of propylthiouracil during pregnancy was previously issued by Health Canada. In light of the above TGA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 16 September 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Canada: Summary Safety Review: Gadolinium-based contrast agents: Assessing the potential risks of congenital anomalies, stillbirth and neonatal death

On 22 September 2021, Health Canada announced that it reviewed the potential risks of congenital anomalies, stillbirth and neonatal death with the use of gadolinium-based contrast agents (GBCAs) during pregnancy. This safety review was initiated following updates made by the United States Food and Drug Administration to the product information for all GBCAs to include the potential risks of stillbirth and neonatal death with the use of these agents during pregnancy.

At the time of the review, the Canadian Product Monographs (CPMs) for GBCAs include warnings to limit the use of these agents during pregnancy unless the potential benefit justifies the potential risk to the fetus, and that the use of a specific type of GBCA may be preferable during pregnancy. The purpose of this review was to assess whether additional warnings or other actions were required in Canada.

GBCAs are classified into 2 types based on their chemical structure: linear agents and macrocyclic agents. In 2019, the majority of GBCAs used in Canada were of the macrocyclic type, which may be preferable in pregnancy. As of 22 September 2021, there were 8 GBCAs authorized for sale in Canada:

- Linear agents: Magnevist (gadopentetate dimeglumine) and 1 generic drug product, MultiHance (gadobenate dimeglumine), Omniscan (gadodiamide), Primovist (gadoxetate disodium)
- Macrocyclic agents: Dotarem (gadoterate meglumine), Gadovist (gadobutrol), ProHance (gadoteridol)

Safety Update

Health Canada reviewed information from searches of the Canada Vigilance database, the World Health Organization's Adverse Drug Reaction Database, and the published literature. At the time of the review, Health Canada had not received any Canadian or international reports of stillbirth nor neonatal death with the use of GBCAs during pregnancy. Health Canada reviewed 3 international case reports of congenital anomalies with the use of GBCAs from the Canada Vigilance database. There were no Canadian reports of congenital abnormalities related to GBCA use at the time of the assessment. The review concluded it was unlikely that congenital anomalies were linked to GBCA use during pregnancy for 1 case, while 2 cases did not have enough information in the reports for further review.

Health Canada also looked at additional information from 7 published studies on the use of GBCAs in pregnancy and congenital anomalies, stillbirth and neonatal death. One large Canadian study found a higher risk of stillbirth or neonatal death with the use of GBCAs during pregnancy. However, it was not possible to conclude there was a link between these potential risks and the use of GBCAs during pregnancy due to weaknesses in the study design. The other 6 studies did not support a link between congenital anomalies, stillbirth, or neonatal death and the use of GBCAs in pregnancy. These studies also had weaknesses in their design.

Health Canada's review of the available information found no link between the use of GBCAs during pregnancy and the risk of congenital anomalies. However, at this time, there is not enough information to rule out a link between the use of GBCAs during pregnancy and the risk of stillbirth and neonatal death. As a precaution, given the potential for serious harm to fetuses and infants, Health Canada will work with the manufacturers of these products to include the potential risks of stillbirth and neonatal death in the CPMs for all GBCAs.

In Hong Kong, there are 10 registered pharmaceutical products which are gadolinium-based contrast agents (GBCAs), namely Dotarem Inj 377mg/ml (Vial) (HK-41578), Dotarem Prefilled Syringes 377mg/ml (HK-41579), Dotagraf Solution For Injection 22.62g/60ml (HK-66545), Dotagraf Solution For Injection 3.77g/10ml (HK-66546) and Dotagraf Solution For Injection 7.54g/20ml (HK-66547) containing meglumine gadoterate, Omniscan Inj 0.5mmol/ml (HK-43493) containing gadodiamide, Gadovist Inj 1mmol/ml (HK-51750) and Gadovist Inj 1mmol/ml (Prefilled Syringe) (HK-57330) containing gadobutrol, Primovist Pre-filled Syringe Inj 0.25mmol/ml (HK-54116) containing sodium gadoxetate, MultiHance Inj 334mg (HK-57789) containing gadobenic acid (as meglumine gadobenate). All products are prescription-only medicines. As of the end of September 2021, the DH had received adverse drug reaction related to Dotarem (3 cases), Omniscan (2 cases), Gadovist (3 cases) and Primovist (one case), but these cases are not related to congenital anomalies, stillbirth or neonatal death. In light of the above Health Canada's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 23 September 2021, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Recall of Povidone-Iodine Swabsticks

On 2 September 2021, the DH endorsed a licensed drug wholesaler, Luen Cheong Hong Ltd. (LCH), to recall all batches of Povidone-Iodine Swabsticks (Hong Kong registration number: HK-48443) from the market as a precautionary measure because the potency may be out of specification.

The DH received notification from LCH on 2 September 2021 that an overseas health authority reported a recall involving a number of batches of the product as the potency was less than its specification. According to LCH, over 20 affected batches were imported and supplied in Hong Kong. As a precautionary measure, LCH voluntarily recalled all batches of the product from the market.

The above product is an antiseptic containing povidine-iodine and is an over-the-counter medicine used for patient pre-operative skin preparation. According to LCH, the product has been supplied to Hospital Authority hospitals, private hospitals, private clinics, community pharmacies, medicine stores as well as exported to Macau.

As of the end of September 2021, the DH had not received any adverse reaction reports in connection with the affected product. A notice was posted on

the Drug Office website on 2 September 2021 to alert the public of the product recall. The DH noted that the recall was completed.

Batch Recall of Rivotril Tablet 2mg

On 13 September 2021, the DH endorsed a licensed drug wholesaler, Roche Hong Kong Limited (Roche), to recall a batch (batch number: 14080021) of Rivotril Tablet 2mg (Hong Kong registration number: HK-57397) from the market as a precautionary measure because incorrect Hong Kong registration number was printed on some boxes of the batch of the product.

The DH received notification from Roche on 13 September 2021 that a customer found an incorrect Hong Kong registration number (HK-57379) on some boxes of a recent delivery of the product. According to Roche, the batch was packed by a local secondary packaging manufacturer and has been supplied to a Hospital Authority hospital, several private doctors, another licensed drug wholesaler and a community pharmacy. As a precautionary measure, Roche voluntarily recalled the product of that batch from the market.

The above product containing clonazepam is a prescription medicine as well as a dangerous drug used for the treatment of epilepsy and seizures. As of the end of September, the DH has not received any adverse reaction reports in connection with the affected product. A notice was posted on the Drug Office website on 13 September 2021 to alert the public of the product recall. The DH noted that the recall was completed.

Recall of Losacor Tablets and Losacor HCT Tablets

On 16 September 2021, the DH endorsed a licensed drug wholesaler, Novartis Pharmaceuticals (HK) Limited (Novartis), to recall all batches of the following four products from the market as a precautionary measure due to the presence of an impurity in the products.

Name of product and Hong Kong registration number:

- Losacor Tablets 50mg (HK-60232)
- Loscaor Tablets 100mg (HK-60234)
- Losacor HCT 50mg-12.5mg Tablets (HK-59806)
- Losacor HCT 100mg-25mg Tablets (HK-59544)

The DH received notification from Novartis on 16 September 2021 of the finding by the overseas manufacturers of the above products that the active pharmaceutical ingredient of the products contains a higher than accepted level of azido impurity. As a precautionary measure, Novartis voluntarily recalled all batches of the products from the market.

Azido impurity is considered a mutagen that can cause a change in the DNA of a cell and may increase the risk of cancer, but the risk of causing cancer in humans is unknown. Overseas drug regulatory authorities have been reviewing the safety impact of azido impurity found in medicinal products. The DH will closely monitor the development of the issue and any safety updates regarding the drug issued by overseas drug regulatory authorities for consideration of any necessary action.

The above products are prescription medicines used to lower blood pressure. According to Novartis, the products have been imported to Hong Kong and supplied to private hospitals, private doctors and community pharmacies as well as re-exported to Macao.

As of the end of September 2021, the DH had not received any adverse reaction reports in connection with the products. A press release was posted on the Drug Office website on 16 September 2021 to alert the public of the product recall. The DH will closely monitor the recall.

Recall of "Champix tablets 0.5 mg and 1 mg" and "Champix tablets 1 mg"

On 27 September 2021, the DH endorsed a licensed drug wholesaler, Pfizer Corporation Hong Kong Limited (Pfizer), to recall a total of five batches of the following two products from the market as a precautionary measure due to the presence of an impurity in the products.

Name of product, Hong Kong registration number, and Batch number:

- Champix tablets 0.5 mg and 1 mg; HK-55462; 00023530, 00026657
- Champix tablets 1 mg; HK-55437; 00023023, 00025603, 00026556

Drug Recall

The DH received notification on 27 September 2021 from Pfizer that the above batches of the products contain a nitrosamine impurity, namely N-nitroso-varenicline, exceeding the accepted level. The above batches were all available in Hong Kong. As a precautionary measure, Pfizer recalled the above batches of the products from the market.

N-Nitroso-varenicline belongs to the nitrosamine class of compounds, some of which are classified as probable or possible human carcinogens, based on laboratory tests such as rodent carcinogenicity studies. Overseas drug regulatory authorities have been reviewing the safety impact of the nitrosamine impurity found in medicinal products. The DH will closely monitor the development of the issue and any safety updates regarding the drug issued by overseas drug regulatory authorities for consideration of any necessary follow-up action.

The above products contain the active ingredient varenicline and are prescription medicines used for smoking cessation. According to Pfizer, the products have been imported to Hong Kong and supplied to Hospital Authority hospitals, clinics of the DH, private hospitals, private doctors, community pharmacies, wholesalers as well as re-exported to Macao.

As of the end of September 2021, the DH had not received any adverse reaction reports in connection with the products. A press release was posted on the Drug Office website on 27 September 2021 to alert the public of the product recall. The DH will closely monitor the recall.

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

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

Update on Drug Office's website: You can now search the newly registered medicines in the past year at http://www.drugoffice.gov.hk/eps/drug/newsNRM60/en/healthcare_providers?pageNoRequested=1.

Details of ALL registered pharmaceutical products can still be found in the Drug Office website at http://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/news_informations/reListRPP_index.html.

Useful Contact

Drug Complaint:

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

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920
Fax: 2319 6319
E-mail: adr@dh.gov.hk
Link: http://www.drugoffice.gov.hk/adr.html
Post: Adverse Drug Reaction and Adverse Event Following Immunization Unit,
Drug Office, Department of Health,
Room 1856, 18/F, Wu Chung House,
213 Queen's Road East,
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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.