Drug News
藥 物 情 報

Issue Number 157

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in November 2022 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

Singapore: Update on nitrosamine impurity in sitagliptin products

On 2 November 2022, the Health Sciences Authority (HSA) announced that a new nitrosamine impurity, Nitroso-STG-19 (also known as NTTP), has recently been detected in trace amounts in sitagliptin products by the manufacturer. These levels were higher than the internationally acceptable limit in only certain samples of the products.

A very conservative approach is used internationally to set limits for nitrosamine impurities in medicines. The acceptable limits are determined based on what is considered reasonably safe if a patient takes the affected medicine every day for a lifetime of 70 years. Therefore, although the trace amounts of NTTP detected were above the international acceptable limit, HSA has assessed that the risk to patients taking the affected sitagliptin medicines is very low.

The company will be making the necessary changes in the manufacturing processes to eliminate or reduce the amount of the impurity to stipulated levels. In the interim period, in consideration of the benefits of the medicines versus the potential risks, HSA is temporarily allowing a higher limit of NTTP in sitagliptin products so that patients can have continued access to these medicines. HSA has assessed that taking the affected sitagliptin medicines containing NTTP at the higher interim limit for an additional short-term exposure during the interim period presents minimal additional risk to patients. While there are other anti-diabetic medicines available, switching patients from sitagliptin to alternative medicines could potentially result in disruption in diabetes control in patients. This could pose greater health risks to patients compared to the low risk of taking the affected products. Patients taking sitagliptin medicines are advised not to stop taking these medicines on their own as sudden stoppage in the use of the medicines can raise blood sugar levels. This approach of HSA's is consistent with those taken by other regulatory authorities.

HSA is working closely with international regulatory agencies and the company supplying these medicines to implement measures to eliminate or reduce the amount of the impurity to acceptable levels.

In Hong Kong, there are 12 registered pharmaceutical products containing sitagliptin. All products are registered by Merck Sharp & Dohme (Asia) Ltd (MSD). They are prescription-only medicines. As of the end of November 2022, the Department of Health (DH) had received 9 cases of adverse drug reaction related to sitagliptin. None of them is concluded to be related to the presence of NTTP.

Related news was previously issued by the Therapeutic Goods Administration in Australia, and was reported in Drug News Issues No. 155. The DH had contacted MSD to follow up on the impact of the local marketed products and to provide evidence that NTTP in the products are below acceptance limit. The DH will remain vigilant on the development of the issue and any safety update of the drug issued by overseas drug regulatory authorities for consideration of any action deemed necessary.

Singapore: Jinarc® (Tolvaptan): New drug for treatment for autosomal dominant polycystic kidney disease (ADPKD) and risk of liver injury

On 4 November 2022, the Health Sciences Authority (HSA) announced that a Dear Healthcare

Professional Letter has been issued by Otsuka Pharmaceuticals (Singapore) Pte Ltd to inform healthcare professionals of the approval of Jinarc® (tolvaptan) for the treatment of autosomal dominant polycystic kidney disease (ADPKD) as well as the risk of liver injury associated with its use.

Jinarc® has been associated with idiosyncratic elevations of blood alanine and aspartate aminotransferases with infrequent cases of concomitant elevations in bilirubin-total. In post-marketing experience with Jinarc® in ADPKD, acute liver failure requiring liver transplantation has been reported. Jinarc® is only available through a restricted distribution programme, which is part of a risk management programme that Otsuka has put in place to manage the risk of idiosyncratic hepatic toxicity associated with the use of Jinarc®. Only prescribers, pharmacies, and patients enrolled in the programme can prescribe, dispense, and receive Jinarc® respectively. Jinarc® treatment must be initiated and monitored under the supervision of physicians with expertise in managing ADPKD and a full understanding of the risks of Jinarc®, including hepatic toxicity and monitoring requirements.

Healthcare professionals are advised to inform their patients about regular blood testing required to monitor and manage the risk of liver injury while taking Jinarc® and to discuss with them the monitoring of symptoms that may indicate liver injury.

In Hong Kong, Jinarc Tablets 30mg (HK-65098), Jinarc Tablets 90mg+30mg (HK-65099), Jinarc Tablets 45mg+15mg (HK-65100), Jinarc Tablets 15mg (HK-65101) and Jinarc Tablets 60mg+30mg (HK-65102) are pharmaceutical products registered by Otsuka Pharmaceutical (HK) Ltd. All products are prescription-only medicines. As of the end of November 2022, the Department of Health (DH) had not received any case of adverse drug reaction related to tolvaptan.

Safety information on the risk of liver injury (including idiosyncratic elevations of blood alanine and aspartate aminotransferases with infrequent cases of concomitant elevations in bilirubin-total and acute liver failure requiring liver transplantation) had already been included in the package insert of Hong Kong registered Jinarc products. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

European Union: EMA confirms measures to minimise risk of serious side effects with Janus kinase (JAK) inhibitors for chronic inflammatory disorders

On 11 November 2022, the European Medicines Agency (EMA) announced that the Committee for Medicinal Products for Human Use (CHMP) has endorsed the measures recommended by the Pharmacovigilance Risk Assessment Committee (PRAC) to minimise the risk of serious side effects with Janus kinase (JAK) inhibitors used to treat several chronic inflammatory disorders. These side effects include cardiovascular conditions, blood clots, cancer and serious infections.

These medicines should be used in the following patients only if no suitable treatment alternatives are available: those aged 65 years or above, those at increased risk of major cardiovascular problems (such as heart attack or stroke), those who smoke or have done so for a long time in the past and those at increased risk of cancer.

JAK inhibitors should be used with caution in patients with risk factors for blood clots in the lungs and in deep veins (venous thromboembolism, VTE) other than those listed above. Further, the doses should be reduced in patient groups who are at risk of VTE, cancer or major cardiovascular problems, where possible.

The recommendations follow a review of available data, including the final results from a clinical trial of the JAK inhibitor Xeljanz (tofacitinib) and preliminary findings from an observational study involving Olumiant (baricitinib). The review also included advice from an expert group of rheumatologists,dermatologists, gastroenterologists and patient representatives.

The review confirmed Xeljanz increases the risk of major cardiovascular problems, cancer, VTE, serious infections and death due to any cause when compared with medicines belonging to the class of TNF-alpha inhibitors. EMA has now concluded that these safety findings apply to all approved uses of JAK inhibitors in chronic inflammatory disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, ulcerative colitis, atopic dermatitis and alopecia areata).

The product information for JAK inhibitors used to treat chronic inflammatory disorders will be

updated with the new recommendations and warnings. In addition, the educational material for patients and healthcare professionals will be revised accordingly.

Information for healthcare professionals:

- An EMA review has found that, compared with TNF-alpha inhibitors, JAK inhibitors used to treat chronic inflammatory disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, ulcerative colitis, atopic dermatitis and alopecia areata) are linked to a higher risk of major adverse cardiovascular events (MACE), VTE, malignancy, serious infections and all-cause mortality.
- The review included the final results from an open-label clinical trial (ORAL Surveillance study) of the JAK inhibitor Xeljanz (tofacitinib) in patients with rheumatoid arthritis and cardiovascular risk factors which found a higher risk of these events with Xeljanz than with TNF-alpha inhibitors.
- Preliminary findings from an observational study (B023) involving another JAK inhibitor, Olumiant (baricitinib), also suggest an increased risk of MACE and VTE in patients with rheumatoid arthritis treated with Olumiant compared with those treated with TNF-alpha inhibitors.
- EMA concluded that the identified risks apply to all JAK inhibitors approved for the treatment of chronic inflammatory disorders.
- These medicines (Xeljanz, Cibinqo, Olumaint, Rinvoq and Jyseleca) should only be used in the following patients if no suitable treatment alternatives are available: those aged 65 years or above, those who are current or past long-time smokers, those with a history of atherosclerotic cardiovascular disease or other cardiovascular risk factors, or those with other malignancy risk factors. Cautious use is also recommended in patients with known risk factors for VTE other than those listed above.
- If JAK inhibitors are needed in patients with these risk factors, a lower dose may be recommended, depending on the medicine, the indication and the specific risk factor.
- Healthcare professionals should discuss the risks associated with JAK inhibitors with their patients.
- It is recommended that healthcare professionals carry out periodic examinations of their patients' skin to check for skin cancer, particularly for patients at risk for skin cancer.

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 2 products containing upadacitinib, namely Rinvoq Prolonged-Release Tablets 15mg (HK-66872) and Rinvoq Prolonged-Release Tablets 30mg (HK-67512) which are registered by Abbvie Limited. All products are prescription-only medicines. There is no registered pharmaceutical product containing abrocitinib or filgotinib.

As of the end of November 2022, the Department of Health (DH) had received adverse drug reaction related to tofacitinib (9 cases; of which 2 cases were related to cancer, 3 cases were related to deep vein thrombosis, one case was related to disseminated tuberculosis, one case was related to cellulitis, one case was related to pneumonia and one case was related to herpes zoster disseminated), baricitinib (3 cases; of which one case was related to deep vein thrombosis, one case was related to pneumocystis jirovecii pneumonia and one case was related to hypotension) and upadacitinib (6 cases; of which 4 cases were related to herpes zoster and one case was related to cytomegalovirus colitis).

Related news on the risk of blood clots, serious heart-related problems, cancer and serious infections of JAK inhibitors was previously issued by various overseas drug regulatory authorities, and was reported in Drug News Issues No. 112, 115, 117, 120, 121, 125, 128, 136, 138, 143, 147, 148, 155 and 156. The DH issued letters to inform local healthcare professionals to draw their attention on 29 July 2019, 19 June 2020, 15 June 2021, 2 September 2021 and 31 October 2022.

In December 2019, the Registration Committee of the Pharmacy and Poisons Board (the Committee) discussed the matter on the risk of blood clots and death associated with the use of tofacitinib, 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).

In December 2021, the Committee discussed the

matter on the risk of venous thromboembolic events (including deep vein thrombosis and pulmonary embolism) associated with the use of JAK inhibitors (tofacitinib, baricitinib and ruxolitinib), and decided that the sales pack or package insert of these products should include the relevant safety information.

As previously reported, the matter will be further discussed by the Committee .

European Union: EMA confirms recommendation to withdraw marketing authorisations for amfepramone medicines

On 11 November 2022, the European Medicines Agency (EMA) announced that the Pharmacovigilance Risk Assessment Committee (PRAC) confirmed its recommendation to withdraw the marketing authorisations for amfepramone obesity medicines on 27 October 2022. This follows a re-examination of its previous recommendation of June 2022, which was requested by the companies that market these medicines.

The recommendation follows a review which found that measures to restrict the use of these medicines for safety reasons have not been sufficiently effective. It found that the medicines were being used for longer than the recommended maximum period of 3 months, thereby potentially increasing the risk of serious side effects such as pulmonary arterial hypertension (high blood pressure in the lungs) and dependency. The medicines were also being used in patients with a history of heart disease or psychiatric disorders, increasing their risk of heart and psychiatric problems. In addition, there was evidence of use during pregnancy, which could pose risks to the unborn baby.

The review considered all available information relating to these concerns, including data from two studies on the use of amfepramone medicines in Germany and in Denmark. In addition, the PRAC received advice from a group of experts, comprising endocrinologists, cardiologists and a patient representative.

The PRAC considered introducing further measures to minimise the risk of side effects but could not identify any that would be sufficiently effective. The PRAC therefore concluded that the benefits of amfepramone medicines do not outweigh their risks and recommended that the medicines be removed from the market in the European Union.

The Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) agreed with the PRAC recommendation and adopted its position by majority on 10 November 2022.

Information for healthcare professionals:

- EMA is recommending the withdrawal of the European Union marketing authorisations for amfepramone medicines for the treatment of obesity.
- A review of available data has found that amfepramone medicines continue to be used outside the current risk minimisation measures included in the product information.
- Inappropriate use may increase the risk of serious adverse effects, including cardiovascular disease, pulmonary arterial hypertension, dependency and psychiatric disorders, as well as harmful effects if used during pregnancy.
- A review of available data also indicates that the efficacy of amfepramone in the treatment of obesity is limited.
- Healthcare professionals should advise patients about other treatment options.

In Hong Kong, there is one registered pharmaceutical product containing amfepramone, namely Dipropion Capsules 75mg (HK-64796). The product is registered by Jean-Marie Pharmacal Co Ltd. It is a prescription-only medicine. As of the end of November 2022, the Department of Health (DH) had not received any case of adverse drug reaction related to amfepramone. Related news was previously issued by EMA, and was reported in Drug News Issues No. 152 and 156.

In light of the above EMA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 14 November 2022, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

European Union: New recommendations for terlipressin-containing medicines in the treatment of hepatorenal syndrome

On 11 November 2022, the European Medicines Agency (EMA) announced that the Pharmacovigilance Risk Assessment Committee (PRAC) recommended new measures to reduce the

risk of respiratory failure and sepsis when using terlipressin-containing medicines in people with type 1 hepatorenal syndrome (type 1 HRS) on 29 September 2022.

The new measures include adding to the product information a warning to avoid using terlipressin-containing medicines in patients with advanced acute-on-chronic liver disease or advanced kidney failure. Patients with breathing problems should receive treatment to manage their condition before starting terlipressin-containing medicines. During and after treatment, patients should be monitored for signs and symptoms of respiratory failure and infection. In addition, healthcare professionals can consider giving terlipressin-containing medicines as a continuous infusion into the vein as an alternative to giving it by bolus injection as this may reduce the risk of severe side effects.

The recommendations follow the PRAC's review of available data, including results from a clinical trial involving patients with type 1 HRS which suggested that patients who were treated with terlipressin-containing medicines were more likely to experience and die from respiratory disorders within 90 days after the first dose than those who were given placebo. Although respiratory failure is a known side effect of terlipressin-containing medicines, the frequency of respiratory failure seen in the study was higher (11%) than previously reported in the product information. In addition, the study reported sepsis in 7% of patients in the terlipressin arm compared with none in the placebo group.

There were limitations to the data, such as differences in how terlipressin was used in the clinical trials compared to clinical practice. After considering these limitations together with other available data and consulting an expert group composed of healthcare professionals with expertise in the field of hepatorenal syndrome, PRAC concluded that new measures were needed to ensure that the benefits of terlipressin-containing medicines continue to outweigh the risks.

The PRAC recommendations were sent to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) which endorsed them and adopted its position on 10 November 2022.

Information for healthcare professionals:

- A higher than previously known risk of respiratory failure has been reported when using terlipressin-containing medicines for the treatment of type 1 HRS). In addition, a new risk of sepsis has been identified with the use of terlipressin-containing medicines for treating this disease.
- Terlipressin-containing medicines should be avoided in patients with advanced renal dysfunction (serum creatinine ≥ 442µmol/l (5.0 mg/dl)) and in patients with acute-on-chronic liver failure grade 3 and/or model for end-stage liver disease (MELD) score ≥39 MELD score, unless the benefits outweigh the risks.
- Patients with new onset of breathing difficulties or worsening of existing respiratory disease should be stabilized before treatment with terlipressin-containing medicines and should be closely monitored during treatment. If patients develop respiratory symptoms, a dose reduction of human albumin should be considered, if applicable. If symptoms are severe or do not resolve, terlipressin-containing medicines should be discontinued.
- Patients should be closely monitored for symptoms of infection.
- In addition, healthcare professionals can consider giving terlipressin-containing medicines as a continuous intravenous infusion as an alternative to bolus injection, as continuous infusion may reduce the risk of severe adverse events compared to bolus injection.

In Hong Kong, there are 4 registered pharmaceutical products containing terlipressin. All products are prescription-only medicines. As of the end of November 2022, the Department of Health (DH) had not received any case of adverse drug reaction related to terlipressin. Related news was previously issued by EMA, and was reported in Drug News Issues No. 147 and 155. The DH issued letters to inform local healthcare professionals to draw their attention on 3 October 2022. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

The United States: FDA investigating risk of severe hypocalcemia in patients on dialysis receiving osteoporosis medicine Prolia (denosumab)

On 22 November 2022, the US Food and Drug Administration (FDA) announced that it is investigating the risk of severe hypocalcemia with serious outcomes, including hospitalization and death, in patients with advanced kidney disease on dialysis treated with the osteoporosis medicine Prolia (denosumab). FDA's review of interim results from an ongoing safety study of Prolia suggests an increased risk of hypocalcemia, or low calcium levels in the blood, in patients with advanced kidney disease. Preliminary results from a separate internal FDA study further investigating hypocalcemia in dialysis patients treated with Prolia show a substantial risk with serious outcomes, including hospitalization and death.

Because of the frequency and seriousness of these risks, FDA is alerting health care professionals and patients about them and is continuing to evaluate this potential safety issue with Prolia use in patients with advanced kidney disease, particularly those on dialysis. FDA will communicate the final conclusions and recommendations when the review is completed and there is more information to share.

Patients should not stop Prolia treatment without first consulting their health care professional, as stopping may worsen their bone condition. Talk to their health care professional about any concerns they may have, including possible alternative treatments. Tell their health care professional if they experience any symptoms of low blood calcium levels such as unusual tingling or numbness in the hands, arms, legs, or feet; painful muscle spasms or cramps; voice box or lung spasms causing difficulty breathing; vomiting; seizures; or irregular heart rhythm.

Health care professionals should consider the risks of hypocalcemia with the use of Prolia in patients on dialysis. When Prolia is used in these patients, adequate calcium and vitamin D supplementation and frequent blood calcium monitoring, possibly more often than is already being conducted, may help decrease the likelihood or severity of these risks. Advise patients on dialysis to immediately seek help if they experience symptoms of hypocalcemia.

When FDA first approved Prolia, it required the manufacturer, Amgen, to conduct a long-term safety study in women with postmenopausal osteoporosis and men with osteoporosis. FDA's review of the interim results from this ongoing safety study suggests an increased risk of hypocalcemia with Prolia in patients with advanced kidney disease. In addition, adverse event reports submitted to FDA showed severe and symptomatic hypocalcemia, including hospitalization and death, is occurring in patients with advanced kidney disease treated with Prolia. Preliminary results from a separate internal FDA study investigating the risk of hypocalcemia suggest that patients on dialysis treated with Prolia are at substantial risk for severe and symptomatic hypocalcemia, including hospitalization and death.

In Hong Kong, Prolia Solution For Injection In Pre-filled Syringe 60mg/ml (USA) (HK-60588) and Prolia Solution For Injection In Pre-filled Syringe 60mg/ml (The Netherlands) (HK-60589) are pharmaceutical products containing 60mg of denosumab which are registered by Amgen Hong Kong Limited. Both products are prescription-only medicines. As of the end of November 2022, the Department of Health (DH) had received 62 cases of adverse drug reaction related to denosumab, of which 3 cases were related to hypocalcemia/serum calcium decreased.

Related news on the risk of hypocalcemia associated with the use of Xgeva (containing 120mg of denosumab) was previously issued by Health Canada and Singapore Health Sciences Authority, and reported in Drug News Issues No. 31 and 59. The DH issued letters to inform local healthcare professionals to draw their attention on 1 June 2012.

In December 2012, the Registration Committee of the Pharmacy and Poisons Board discussed the matter for Xgeva and Prolia, and decided that the sales pack label and/or package insert of denosumab products should include safety information about the risk of hypocalcemia (including in patients with severe renal impairment or receiving dialysis). The DH will remain vigilant on the conclusion of the review and any safety updates issued by other overseas drug regulatory authorities.

The United Kingdom: Dupilumab (Dupixent): risk of ocular adverse reactions and need for prompt management

On 29 November 2022, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that healthcare professionals prescribing dupilumab should be alerted to the risk of ocular

adverse reactions and need for prompt management.

The potential for adverse reactions affecting the eye with dupilumab was established in the initial clinical trials. Further ocular adverse reactions have been identified during post-marketing clinical use. Although most ocular reactions are mild, some can become serious. MHRA has received a small number of Yellow Card reports of ulcerative keratitis with serious corneal damage associated with dupilumab treatment.

MHRA recently reviewed the risk of dry eye and also serious ocular side effects associated with dupilumab. The review recommended that updates should be made to the product information for dupilumab to include the adverse drug reaction 'dry eye' and also to emphasise the need for prompt and appropriate management of any potential ocular reactions. It is not currently possible to predict who may experience the rarer and most serious ocular adverse reactions, such as ulcerative keratitis. It is therefore important, with all ocular reactions, for patients to receive prompt care, with treatment provided as appropriate to prevent or minimise damage to the eye.

MHRA is also alerting healthcare professionals prescribing tralokinumab. Clinical trial data have indicated that keratitis, conjunctivitis and allergic conjunctivitis are associated with tralokinumab use. MHRA is advising healthcare professionals prescribing dupilumab and tralokinumab to discuss with patients the potential for side effects affecting the eye and to ensure any reactions are managed promptly, especially in a patient experiencing eye pain or changes to their vision.

Up to 7 September 2022, MHRA has received 479 reports in the United Kingdom which included suspected ocular side effects with dupilumab. 111 of these reports were considered serious. 9 reports of ulcerative keratitis were received, representing 5 cases (for some individual cases, MHRA received more than one report from different sources). 2 of these cases involved corneal perforation. 18 reports involved children ranging from 6 to 17 years of age. With regards to the ocular events listed for dupilumab, please refer to the website in MHRA for details of the number of reports in the United Kingdom received by MHRA.

Up to 7 September 2022, MHRA has received no ocular related reports regarding tralokinumab.

Patients with atopic dermatitis commonly present with ocular surface diseases such as allergic conjunctivitis, blepharitis, and keratitis, as well as infectious conjunctivitis and keratoconus (changes to the shape of the cornea). The mechanisms by which dupilumab or tralokinumab increase the occurrence of, or exacerbate, ocular adverse events are not fully understood. Publications, including individual case reports about patients experiencing suspected ocular side effects with dupilumab, show variability in timing of onset and progression, presentation, and sequelae of ocular adverse reactions. In most reports received by MHRA where patients have experienced ocular adverse reactions with dupilumab, the reactions have not been considered to be serious by the reporter. However, MHRA has received 9 reports of 5 patients who experienced ulcerative keratitis with dupilumab, and, where the information was provided, treatment required corneal gluing or tectonic keratoplasty. The details of some of the serious reports, and expert advice, indicate that early review and intervention are beneficial to the patient.

Expert ophthalmology and dermatology advice provided to MHRA indicated that in clinical experience in the United Kingdom, most ocular reactions seen with dupilumab are mild and can be managed. However, it is not currently possible to predict who may experience the rarer and most severe ocular adverse reactions, such as ulcerative keratitis. It is therefore important, with all ocular reactions, for patients to receive prompt care, with treatment provided as appropriate to prevent or minimise damage to the eye. It is important to recognise 'red flags' for urgent ophthalmological consultation, such as eye pain, vision loss, and an increase in ocular pressure.

Advice for healthcare professionals:

- Dupilumab is commonly associated with cases of conjunctivitis and allergic conjunctivitis, eye pruritus, blepharitis, and dry eye and with infrequent cases of keratitis and ulcerative keratitis, especially in patients with atopic dermatitis.
- Be alert to the risks of ocular reactions and promptly review new onset or worsening ocular symptoms, referring patients for ophthalmological examination as appropriate. Sudden changes in vision or significant eye pain that does not settle warrant urgent review.
- Discuss with patients or caregivers the potential for, and symptoms of, ocular side

Safety Update

effects at initiation of dupilumab, including symptoms of conjunctivitis and dry eye (which can also include paradoxical eye watering), keratitis and ulcerative keratitis.

- Advise patients to promptly report new-onset or worsening eye symptoms to their healthcare professional so that appropriate treatment can be initiated. Advise patients not to self-manage ocular symptoms.
- Ensure that patients who develop conjunctivitis or dry eye that does not resolve following initial treatment, or patients with signs and symptoms suggestive of keratitis (especially eye pain and vision changes), undergo ophthalmological examination, as appropriate.

- MHRA reminds healthcare professionals that tralokinumab (Adtralza), another interleukin-13 inhibitor recently licenced for use in atopic dermatitis, is also associated with common cases of conjunctivitis and allergic conjunctivitis as well as uncommon cases of keratitis, and that patients treated with tralokinumab who develop conjunctivitis that does not resolve following standard treatment should undergo ophthalmological examination.

In Hong Kong, there are 2 registered pharmaceutical products containing dupilumab, namely Dupixent Solution For Injection In Pre-filled Syringe 300mg/2ml (HK-65961) and Dupixent Solution For Injection In Pre-filled Syringe 200mg/1.14ml (HK-66635). Both products are registered by Sanofi Hong Kong Limited. They are prescription-only medicines. There is no registered pharmaceutical product containing tralokinumab. As of the end of November 2022, the Department of Health had received 8 cases of adverse drug reaction related to dupilumab, of which one case was related to vision abnormal and one case was related to corneal ulcer. In light of the above MHRA's announcement, The DH issued letters to inform local healthcare professionals to draw their attention on 30 November 2022, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Batch recall of Allergenic Extract for diagnostic test – Peanut

On 22 November 2022, the Department of Health (DH) endorsed licensed wholesaler, Ksena Healthcare Limited (Ksena), to recall a batch (lot number 0004014634) of skin test reagent for allergy to peanut, namely Allergenic extract – Peanut due to potential quality issue.

The DH received notification from Ksena that the overseas manufacturer has recalled the skin test reagent due to reports of individuals who were test-negative using the above product lot subsequently experienced allergic reactions to peanut. As a precautionary measure, Ksena voluntarily recall the affected batch. DH investigation is continuing.

The above product is a skin test reagent for allergy to peanut, the product was unregistered but imported for named patient use by registered medical practitioner through Ksena. The DH will closely monitor the recall. Health-care professionals who have the product in hand should return the product to the supplier.

As of the end of November 2022, the DH had not received any adverse reaction reports in connection with the above batch of product. A notice was posted on the Drug Office website on 22 November 2022 to alert the public of the product recall. The DH noted that the recall was completed.

Drug Incident

Public urged not to buy or use topical product containing undeclared controlled ingredient

On 17 November 2022, the Department of Health (DH) appealed to the public not to buy or use a topical product (labelled as "草本護膚膏" with no English name) as it was found to contain an undeclared controlled drug ingredient.

Acting upon a public complaint, the DH collected a sample of the above product from a premises in Wan Chai for analysis. The test result from the Government Laboratory revealed that the product sample contained triamcinolone acetonide, which is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138). The product is also suspected to be an unregistered pharmaceutical

product.

The DH conducted an operation against the above premises on 17 November 2022. During the operation, two women aged 45 and 60 were arrested by the Police for suspected illegal sale of a Part 1 poison and unregistered pharmaceutical product. The DH's investigation is continuing.

Triamcinolone acetonide is a steroid substance for treating inflammation. Inappropriate application of steroids could cause skin problems and systemic side effects such as moon face, high blood pressure, high blood sugar, adrenal insufficiency and osteoporosis. Products containing triamcinolone acetonide are prescription medicines that should be used under a doctor's directions and be supplied in a pharmacy under the supervision of a registered pharmacist upon a doctor's prescription.

A press release was posted on the Drug Office website on 17 November 2022 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 $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.

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: 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,
Wanchai, 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.