Drug News
藥 物 情 報

Issue Number 168

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in October 2023 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

Australia: Use caution when prescribing baclofen off-label

On 19 October 2023, the Therapeutic Goods Administration (TGA) announced that recent coronial inquiries into 2 deaths have highlighted the need for health professionals to be alert to the well documented risk of overdose with baclofen. This risk relates to intentional and unintentional overdose and is particularly pronounced when baclofen is used off-label at higher doses for alcohol-use disorder.

The registered indication for baclofen is for the suppression of voluntary muscle spasm in multiple sclerosis; and spinal lesions of traumatic, infectious, degenerative, neoplastic and unknown origin causing skeletal hypertonus, spastic and dyssynergic bladder dysfunction.

The Product Information (PI) and Consumer Medicine Information (CMI) for baclofen products include warnings about the risk of suicide and suicide-related events, recommending close supervision of patients with alcohol-use disorder, depression and/or a history of previous suicide attempts. The optimum dosage listed in the PI ranges from 30 to 75 mg daily, although occasionally doses up to 100 mg daily may be necessary in hospitalised patients. Higher dosages may be recommended for off-label use in treating alcohol-use disorder.

Health professionals should be alert to the risk of overdose (intentional and unintentional) in patients taking baclofen off-label for alcohol-use disorder. Baclofen overdose is potentially fatal. If prescribing baclofen off-label, it is important to obtain informed consent from the patient after a discussion about the benefits and risks of the medicine, particularly at higher doses. Patients (and their carers) should be alerted to the need to monitor for clinical worsening, suicidal behaviour or thoughts, or unusual changes in behaviour. Medical advice should be sought immediately if these symptoms occur.

A search of TGA's Database of Adverse Event Notifications on 28 September 2023 using search term 'baclofen', 'overdose' and 'off-label use' retrieved 43 cases of overdose reported (with 23 cases as single suspect); and 22 cases with off-label use reported (with 6 cases as single suspect).

This safety update is only applicable to the tablet form of baclofen, not baclofen for intrathecal injection.

In Hong Kong, there are 10 registered pharmaceutical products which are baclofen tablets. All products are prescription-only medicines. As of the end of October 2023, the Department of Health (DH) had received 3 cases of adverse drug reaction related to baclofen, but these cases were not related to overdose. In light of the above TGA's announcement, , the DH issued letters to inform local healthcare professionals to draw their attention on 20 October 2023, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board .

European Union: GLP-1 receptor agonists: available evidence not supporting link with thyroid cancer

On 27 October 2023, the European Medicines Agency (EMA) announced that its safety committee, the Pharmacovigilance Risk Assessment Committee (PRAC), has concluded that the available evidence does not support a causal association between the Glucagon-Like Peptide-1 (GLP-1) receptor agonists (exenatide, liraglutide,

dulaglutide, semaglutide and lixisenatide) and cancer of the thyroid (a small gland in the front and lower part of the neck which makes and releases hormones).

GLP-1 receptor agonists are used to treat type 2 diabetes and, in some cases, for the treatment of obesity and overweight under certain conditions. The PRAC began assessing this safety signal following the publication of a study suggesting that there might be an increased risk of thyroid cancers with the use of these medicines in patients with type 2 diabetes mellitus.

The committee reviewed evidence from the published literature, including observational studies, as well as cumulative data submitted by the marketing authorisation holders which included non-clinical, clinical and post-marketing data. At present, the PRAC considers that no updates to the product information are warranted based on the available data.

In Hong Kong, there are registered pharmaceutical products containing dulaglutide (4 products), exenatide (1 product), liraglutide (4 products), lixisenatide (2 products) and semaglutide (11 products). All products are prescription-only medicines. As of the end of October 2023, the Department of Health (DH) had received adverse drug reaction on dulaglutide (5 cases), exenatide (2 cases), liraglutide (1 case), lixisenatide (1 case) and semaglutide (3 cases), but these cases were not related to thyroid cancer. The DH will remain vigilant on safety update of the drugs issued by other overseas drug regulatory authorities.

The United Kingdom: Isotretinoin (Roaccutane): introduction of new safety measures, including additional oversight of the initiation of treatment for patients under 18 years of age

On 31 October 2023, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that it has strengthened the safe use of isotretinoin through the introduction of additional oversight of the initiation of isotretinoin in patients under 18 years and through improved assessment and monitoring of mental health and sexual function issues.

In April 2023, the Commission on Human Medicines (CHM) published recommendations following its review of mental health and sexual side effects suspected to be associated with isotretinoin. The review considered all the available evidence, including information from patients and their families, and recommended new measures to strengthen the safety of isotretinoin treatment.

The product information for isotretinoin medicines has been updated following the review's recommendations. This includes the addition of new warnings and precautions on potential mental health and sexual function side effects to the product information and the requirement for 2 healthcare professionals to agree that there is no other appropriate effective treatment in patients under 18 years of age.

Following its review, the CHM formed an Isotretinoin Implementation Advisory Expert Working Group, composed of experts and representatives of the healthcare organisations to advise on how best to implement the recommendations in clinical practice. The CHM endorsed the guidance from the Isotretinoin Implementation Advisory Expert Working Group.

The Isotretinoin Implementation Advisory Expert Working Group has worked with MHRA to develop guidance specifying which healthcare professionals have the appropriate expertise to be the Lead Prescriber (who makes the decision to initiate isotretinoin treatment); Second Approved Named Healthcare Professional (who agrees that isotretinoin is the most appropriate treatment option for adolescents under 18 years of age); and Follow-Up Prescriber (responsible for continuing and monitoring isotretinoin treatment). The Lead Prescriber must have expertise in the use of systemic retinoids for the treatment of severe acne and a full understanding of the risks of isotretinoin therapy and monitoring requirements. The Isotretinoin Implementation Advisory Expert Working Group also developed guidance on the assessment and monitoring of mental health and sexual function.

New compulsory regulatory risk minimisation materials have been developed for use with all patients consisting of an Acknowledgement of Risk Form, a Patient Reminder Card and a Pharmacist Checklist. These are available electronically and will be sent to relevant healthcare professionals by post.

The Acknowledgment of Risk Form must be completed with all patients initiating isotretinoin

Safety Update

treatment. The new Acknowledgment of Risk Form has been developed to continue to record the patient's acknowledgment of the known risk of harm to unborn babies during pregnancy; record acknowledgment of other risks including possible mental health and sexual function side effects; continue to record enrolment onto the revised Pregnancy Prevention Programme if the patient is of childbearing potential; and record the agreement of 2 independent healthcare professionals that there is no other appropriate effective treatment in patients under 18 years of age.

Advice for healthcare professionals:

- All patients must be counselled about the benefits and risks of treatment before isotretinoin is prescribed, including possible mental health and sexual function side effects; MHRA also asks the referrer (usually the general practitioner) to provide information about isotretinoin to the patient and provide counselling (where possible) regarding the benefits and risks of isotretinoin treatment.
- Isotretinoin is teratogenic; all patients of childbearing potential must be entered into the Pregnancy Prevention Programme.
- Prescribers should assess patients' mental health before prescribing isotretinoin including the use of patient-reported outcome measures.
- Ask patients about any sexual function concerns before prescribing isotretinoin.
- Give the patient sufficient time to consider, reflect and ask questions before starting isotretinoin treatment.
- Use the new regulatory risk minimisation materials with all patients: Acknowledgement of Risk Form, Patient Reminder Card and Pharmacist Checklist.
- The Lead Prescriber, who initiates isotretinoin treatment, must have expertise in the use of systemic retinoids for the treatment of severe acne and a full understanding of the risks of isotretinoin therapy and monitoring requirements.
- Initiation of isotretinoin treatment in patients under 18 years of age now requires agreement by 2 independent healthcare professionals that there is no other appropriate effective treatment before it is prescribed. This means that isotretinoin should only be prescribed for severe acne that is resistant to adequate courses of standard therapy.
- Review patients approximately 1 month after initiation of treatment in a face-to-face (in-person) appointment.
- Monitor patients for side effects including mental health and sexual function side effects at each follow up appointment including objective mental health patient reported outcome measures.
- Any healthcare professional involved in the treatment of patients with acne, particularly prescribers of isotretinoin, should review the full details of the new requirements in the Report of The Commission on Human Medicines Isotretinoin Implementation Advisory Expert Working Group.

In Hong Kong, there are 11 registered pharmaceutical products containing isotretinoin. All products are prescription-only medicines. As of the end of October 2023, the Department of Health (DH) had received 2 cases of adverse drug reaction on isotretinoin, but these cases were not related to mental health or sexual function side effects.

Related news was previously issued by MHRA, and was reported in the Drug News since Issue No. 96, with the latest update reported in Drug News Issue No. 162. The DH issued letters to inform local healthcare professionals to draw their attention on 27 October 2017 and 27 April 2023.

Currently, the sales pack or package insert of locally registered isotretinoin-containing products should include warnings on suicide, suicidal attempts and sexual dysfunction including erectile dysfunction and decreased libido. As previously reported, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Batch recall of Seirogan Toi A Sugar Coated Tablet

On 4 October 2023, the Department of Health (DH) endorsed a licensed drug wholesaler, Taiko Pharmaceutical (Asia Pacific) Co., Limited (Taiko), to recall a batch (batch number: 41QC1) of Seirogan Toi A Sugar Coated Tablet (Hong Kong registration number: HK-19878) from the market due to potential quality issue.

The DH received notification from Taiko that the

Drug Recall

overseas manufacturer of the product is recalling the above batch because there was deviation noted in the preparation method of one of the product's active ingredient, i.e. Phellodendron bark dried extract, from the supplier. Although the product's manufacturer confirmed that the product has passed all tests during release, the affected batch is voluntarily recalled as a precautionary measure.

The above product, containing Phellodendron bark dried extract, creosote and geranium herb, is an over-the-counter medicine indicated for relief of occasional diarrhea. According to Taiko, the above batch of product has been supplied to local pharmacies, medicine stores and re-exported to Macau.

As of the end of October 2023, the DH had not received any adverse drug reaction report related to the affected batch of product. A recall notice was posted in the Drug Office website on 4 October 2023 to alert the public of the product recall. The DH will closely monitor the recall.

Batch recall of PROSOME Enteric Coated Tablets 20mg

On 10 October 2023, the Department of Health (DH) endorsed a licensed drug wholesaler, Julius Chen & Company (HK) Limited (Julius Chen), to recall a batch (batch number: 1012220026) of PROSOME Enteric Coated Tablets 20mg (Hong Kong Registration Number: HK-58864) from the market due to a quality issue.

In the course of a routine market surveillance by the DH, samples of the product from the above batch were collected for analysis. Test results from the Government Laboratory showed that the samples had failed the disintegration test. Julius Chen was informed of the test result and thus recalled the relevant batch of product from the market. The DH's investigation is continuing.

The above product, containing esomeprazole, is a prescription-only medicine indicated for peptic ulcer disease and gastro-oesophageal reflux disease. According to Julius Chen, the product has been supplied to local pharmacies and private doctors.

As of the end of October 2023, the DH had not received any adverse reaction reports in connection with the above product. A press release was posted in the Drug Office website on 10 October 2023 to alert the public of the product recall. The DH will closely monitor the recall.

Drug Incident

Woman arrested for illegal sale and possession of unregistered pharmaceutical products and Part 1 poisons

On 17 October 2023, the Department of Health (DH) conducted an operation against a retail shop in Yau Ma Tei for suspected illegal sale and possession of unregistered pharmaceutical products and Part 1 poisons. A 32-year-old woman was arrested by the Police during the operation.

Upon intelligence, a retail shop in Yau Ma Tei was found selling some unregistered pharmaceutical products and Part 1 poisons, including pain killers and cough and cold medicines.

Preliminary investigation indicated that, among the 20 types of products seized during the enforcement operation, many contained Part 1 poisons under the Pharmacy and Poisons Ordinance (Cap. 138) (the Ordinance) (including ibuprofen, dihydrocodeine, dextromethorphan, prednisolone, triamcinolone acetonide, felbinac, ketoprofen, hyoscine, tranexamic acid and miconazole). All the products did not bear Hong Kong registration numbers for pharmaceutical products and were labelled in foreign languages (including Japanese and English). The DH's investigation is ongoing.

Ibuprofen is a non-steroidal anti-inflammatory pain killer and its side effects include nausea, gastrointestinal discomfort and peptic ulcers. Dihydrocodeine is an opioid analgesic and may cause nausea, vomiting and constipation. Dextromethorphan is a cough suppressant used for the relief of non-productive cough and adverse effects may include dizziness and gastrointestinal disturbances. Prednisolone and triamcinolone acetonide are steroid substances for treating inflammation. Inappropriate use of steroids could cause skin problems and systemic side effects such as moon face, high blood pressure, high blood sugar, adrenal insufficiency and osteoporosis. Felbinac and ketoprofen are non-steroidal anti-inflammatory drugs which could be used topically to relieve pain. Inappropriate use of

felbinac and ketoprofen may cause erythema and dermatitis. Hyoscine is used in the management of nausea and vomiting. Common side effects of hyoscine include dry mouth, blurred vision and constipation. Tranexamic acid is used in the treatment and prophylaxis of haemorrhage and can cause gastrointestinal disturbances, and inappropriate use may cause cerebral thrombosis. Miconazole is used for the treatment of fungal infections with side effects including local irritation and sensitivity reactions. Products containing the above ingredients should only be supplied by a pharmacy under the supervision of a registered pharmacist. Certain products could only be supplied upon a doctor's prescription.

A press release was posted in the Drug Office website on 18 October 2023 to alert the public of the drug incident.

Man arrested for suspected illegal sale and possession of products with undeclared controlled and banned drug ingredient

On 24 October 2023, the Department of Health (DH) conducted an operation against the sale of two products, namely KetoDiet Coffee and S·Factor Mocha Latte, which were found to contain an undeclared controlled and banned drug ingredient. During the operation, a 41-year-old man was arrested by the Police for suspected illegal sale and possession of Part 1 poisons.

Acting upon intelligence, samples of the above products were purchased from a shop in Fo Tan for analysis. Test results from the Government Laboratory revealed that the samples contained sibutramine, which is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138) (the Ordinance). The DH's investigation is continuing.

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

A press release was posted in the Drug Office website on 24 October 2023 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/

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.