Drug News
藥 物 情 報

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This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in October 2024 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

European Union: EMA has started a review of medicinal products containing finasteride and dutasteride

On 4 October 2024, the European Medicines Agency (EMA) announced that the Pharmacovigilance Risk Assessment Committee (PRAC), has started a review of medicines containing finasteride and dutasteride following concerns regarding suicidal ideation (suicidal thoughts) and behaviours.

Tablets containing 1 mg of finasteride and finasteride solution for application to the skin are used to treat the early stages of androgenic alopecia (hair loss due to male hormones) in men aged 18 to 41 years. Tablets containing 5 mg finasteride and capsules containing 0.5 mg dutasteride are used to treat men with benign prostatic hyperplasia (BPH), a condition in which the prostate is enlarged and can cause problems with the flow of urine.

During the review, PRAC will assess all available data linking finasteride and dutasteride to suicidal ideation and behaviours. It will also evaluate the impact of suicidal ideation and behaviours on the benefit-risk balance of these medicines, taking into consideration the conditions they are used to treat.

Medicines containing finasteride and dutasteride taken by mouth have a known risk of psychiatric side effects, including depression. Suicidal ideation has also recently been added as a possible side effect of unknown frequency in the product information for Propecia and Proscar, the first two finasteride-containing medicines authorised in several countries of the European Union (EU). To minimise the risks, measures are already in place for finasteride medicines, including warnings in the product information for healthcare professionals to monitor patients for psychiatric symptoms and stop treatment if symptoms occur, and recommendations for patients to seek medical advice if they experience psychiatric symptoms.

EMA will now review all available data on suicidal ideation and behaviours with finasteride and dutasteride and issue a recommendation on whether the marketing authorisations for these medicines should be maintained, varied, suspended or withdrawn across the EU.

In Hong Kong, there are 31 and 9 registered pharmaceutical products containing finasteride and dutasteride respectively. All products are prescription-only medicines. As of the end of October 2024, the Department of Health (DH) had received 5 cases of adverse drug reaction related to finasteride and 4 cases of adverse drug reaction related to dutasteride, but these cases were not related to suicidal ideation and behaviours.

Related news on the risk of psychiatric side effects associated with the use of finasteride was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News since Issue No. 91, with the latest update reported in Drug News Issue No. 174. The DH issued letters to inform local healthcare professionals to draw their attention on 25 May 2017 and 20 January 2023. In September 2017 and April 2024, the Registration Committee of the Pharmacy and Poisons Board discussed the matter and in September 2017, the Committee decided that the sales pack label and/or package insert of finasteride-containing products should include the relevant safety information. The DH will remain vigilant on the review started by EMA and any safety update of the drugs issued by other overseas drug regulatory authorities for consideration of any action deemed necessary.

European Union: New safety information for healthcare professionals: risk of medication errors due to change of dosing syringe for Keppra and Levetiracetam UCB oral solution

On 4 October 2024, the European Medicines Agency (EMA) announced that the Pharmacovigilance Risk Assessment Committee (PRAC) discussed a direct healthcare professional communication (DHPC) regarding a change to the dosing syringe included in the product packaging of Keppra and Levetiracetam UCB 100 mg/ml oral solution intended for use in children aged 6 months to 4 years (150 ml bottle). The 3 ml dosing syringe is being replaced with a 5 ml dosing syringe. The DHPC will inform healthcare professionals of the potential risk of medication errors due to the change in the volume of the dosing syringe.

Keppra and Levetiracetam UCB are medicines used to treat epilepsy, on their own or as an add-on to another anti-epileptic medicine.

When prescribing and dispensing levetiracetam (Keppra and Levetiracetam UCB) oral solution with the new 5 ml syringe, healthcare professionals should inform caregivers about the change in the volume of the dosing syringe. Caregivers should be informed that while the new 5 ml syringe is graduated every 0.1 ml, it has additional graduations of 0.25 ml compared to the 3 ml syringe. Caregivers should be counselled on the correct dose and how to measure it with the 5 ml syringe. Caregivers should be advised to read the instructions in the package information leaflet on how to recognise signs and symptoms of a levetiracetam overdose and what to do in this situation.

The DHPC for Keppra and Levetiracetam UCB will be forwarded to EMA's human medicines committee (CHMP). When adopted, the DHPC will be disseminated to healthcare professionals by the marketing authorisation holders, according to an agreed communication plan, and published on the Direct healthcare professional communications page and in national registers in EU Member States.

In Hong Kong, there are 5 registered pharmaceutical products containing levetiracetam in oral solution, including Keppra Oral Solution 100mg/ml (HK-54926) registered by Glaxosmithkline Limited. All products are prescription-only medicines. Levetiracetam UCB is not a registered pharmaceutical product in Hong Kong. As of the end of October 2024, the Department of Health (DH) had received 7 cases of adverse drug reaction with regard to levetiracetam, but these cases were not related to medication errors. Healthcare providers and patients are advised to follow the instructions in package insert regarding the administration with oral syringe.

The United Kingdom: Bromocriptine: monitor blood pressure when prescribing bromocriptine for prevention or inhibition of post-partum physiological lactation

On 24 October 2024, the Medicines and Healthcare products Regulatory Agency (MHRA) announced that a safety review has been conducted by the MHRA following a Yellow Card report concerning a patient who was taking bromocriptine. The review concluded that blood pressure monitoring of patients prescribed with this drug is essential especially during the first days of treatment.

The MHRA has received a Yellow Card report which highlighted the need for blood pressure monitoring during bromocriptine treatment, especially during the first days of therapy. It is imperative that signs and symptoms of hypertension are recognised in patients receiving bromocriptine. Treatment with bromocriptine should be discontinued in hypertensive patients or when signs and symptoms of hypertension are detected and the patient promptly evaluated with consideration given as to whether they should be referred for further investigation and management of high blood pressure or close monitoring.

Advice for healthcare professionals:

- Bromocriptine should only be prescribed to suppress post-partum physiological lactation, where it is medically indicated such as intrapartum loss, neonatal death, or in some cases of HIV infection of the mother.
- Bromocriptine should not be used for routine lactation suppression, or for relieving symptoms of postpartum breast pain and engorgement, which can be adequately treated with non-pharmacological interventions (such as firm breast support, ice application) and simple analgesics.
- Use is contraindicated for patients with uncontrolled hypertension, hypertensive disorders of pregnancy (including eclampsia, pre-eclampsia or pregnancy-induced hypertension), hypertension post-partum and

in the puerperium, a history of coronary artery disease or other severe cardiovascular conditions.

- Particular caution is required in patients who are on concomitant therapy or recent treatment with drugs that can alter blood pressure.
- When prescribing bromocriptine for any of its indications, carefully monitor for an increase in blood pressure, especially during the first days of therapy and with any subsequent dose increases.
- If patients prescribed bromocriptine present with signs and symptoms of hypertension, treatment should be discontinued, and the patient evaluated promptly by healthcare professionals.
- Clinical guidance recommends cabergoline as the preferred drug for prevention or inhibition of post-partum physiological lactation, owing to the single dose regime and lower rates of rebound breast activity and adverse events. However, blood pressure monitoring is still necessary when taking cabergoline as both cabergoline and bromocriptine are dopamine agonists and should not be given to women with hypertension or pre-eclampsia.
- Healthcare professionals are encouraged to read the Summary of Product Characteristics (SmPC) for special warnings and contraindications for the use of bromocriptine and cabergoline.

In Hong Kong, there are 5 and 2 registered pharmaceutical products containing bromocriptine and cabergoline respectively. All products are prescription-only medicines. As of the end of October 2024, the Department of Health (DH) had not received any adverse drug reaction with regard to bromocriptine and cabergoline.

Related news associated with the use of bromocriptine was previously issued by European Medicines Agency, Health Sciences Authority, Taiwan Food and Drug Administration and National Medical Products Administration, and was reported in the Drug News since Issue No. 57, with the latest update reported in Drug News Issue No. 70. The DH issued letters to inform local healthcare professionals to draw their attention on 14 July 2014. In February 2015, the Registration Committee of the Pharmacy and Poisons Board discussed the matter and decided that the sales pack label and/or package insert of bromocriptine-containing products should include the relevant safety information. Safety information on blood pressure monitoring and should not be given to women with hypertension or pre-eclampsia has already been included in the package insert of Hong Kong registered cabergoline-containing products. The DH will remain vigilant on safety update of the drugs issued by other overseas drug regulatory authorities.

Australia: Shingrix vaccine and very rare risk of Guillain-Barré Syndrome

On 29 October 2024, the Therapeutic Goods Administration (TGA) announced that it has received Australian reports of Guillain-Barré Syndrome (GBS) following Shingrix vaccination.

After investigating this issue and seeking advice from an expert panel, the Product Information (PI) and Consumer Medicine Information (CMI) documents for Shingrix were updated. These changes reflect the new reporting data, recognising that GBS is a very rare adverse event. The TGA began an investigation into the possible association between Shingrix and GBS in February 2024 after receiving two reports detailing this adverse event.

The Shingrix PI already contained information about an observational study in people aged 65 years and over. The study found an increased risk of GBS (estimated 3 excess cases per million doses administered) observed in the 42 days following vaccination. The PI noted that the evidence was insufficient to determine a causal relationship.

At the time, GBS following Shingrix vaccination had also been reported to the World Health Organisation's global adverse event reports database. The TGA also identified published literature that suggested a possible association between Shingrix and GBS. Its investigation recommended that GBS be included in the adverse event section of the Australian Shingrix PI. This update harmonises the Australian PI with corresponding information from the United States and Canada.

The association between GBS and Shingrix was also considered by an independent expert advisory group on immunisation. This review included discussion of a single adverse event report involving Shingrix and meningoencephalitis. The expert group agreed that inclusion of GBS as an adverse event in the Shingrix PI was appropriate and recommended raising awareness of the possibility of GBS following Shingrix.

The TGA's public Database of Adverse Event Notifications included 13 reports of GBS following Shingrix vaccination up to 18 September 2024. The reports involved patients of both sexes. All were aged from their mid-60s to mid-80s. No deaths were reported.

Healthcare professionals should be aware of GBS cases following vaccination with Shingrix. Patients should be warned of this possible but very rare risk and encouraged to seek medical attention if they experience symptoms, as early medical care can reduce severity and improve outcomes.

Shingrix is not generally recommended for people with a history of GBS whose first episode occurred within 6 weeks of receiving any vaccine (such as an influenza vaccine or a previous dose of Shingrix vaccine). Those with a history of GBS not associated with Shingrix should discuss the risks and benefits of receiving Shingrix with a healthcare professional.

Symptoms of GBS include pins and needles (paraesthesia), numbness, weakness and paralysis. Typically, hands and/or feet are affected first, with symptoms progressing up the body to the legs, arms, face and muscles involved with breathing. These symptoms may progress over a few days or weeks.

In Hong Kong, Shingrix Vaccine Powder And Suspension For Suspension For Injection (HK-66840) is a pharmaceutical product registered by GlaxoSmithKline Limited, and is a prescription-only medicine. As of the end of October 2024, the Department of Health (DH) had received 4 cases of adverse events following immunisation with Shingrix, but these cases were not related to GBS.

Related news was previously issued by the US Food and Drug Administration, and was reported in Drug News Issue No. 137. The DH issued letters to inform local healthcare professionals to draw their attention on 25 March 2021. In February 2022, the Registration Committee of the Pharmacy and Poisons Board discussed the matter, and decided that the sales pack labels and/or package inserts of locally registered Shingrix vaccine should include the relevant safety information about increased risk of Guillain-Barré syndrome in individuals aged 65 years or older. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Singapore: Gavreto (pralsetinib): New warning and precaution of severe and fatal infections

On 29 October 2024, the Health Sciences Authority (HSA) announced that a Dear Healthcare Professional Letter has been issued by Roche Singapore Pte Ltd to update healthcare professionals that severe and fatal infections, including opportunistic infections, have been reported in patients treated with Gavreto. An ad hoc analysis of results from the ongoing phase III trial AcceleRET-Lung demonstrated an imbalance regarding the risk of severe and fatal infection, including severe opportunistic infections, between the pralsetinib and standard of care arms. Healthcare professionals are advised to monitor patients closely for signs and symptoms of infection and treat appropriately. They are also advised to withhold Gavreto in the presence of active infection and discontinue Gavreto permanently if infections are life-threatening.

In Hong Kong, there is one registered pharmaceutical product containing pralsetinib, namely Gavreto Capsules 100mg (HK-67499). The product is registered by Cstone Pharm (HK) Holding Limited. It is a prescription-only medicine. As of the end of October 2024, the Department of Health (DH) had received 2 cases of adverse drug reaction with regard to pralsetinib, of which one case was reported as pneumonia (lung infection). In light of the above HSA's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 30 October 2024. The DH will remain vigilant on safety update of the drug issued by other overseas drug regulatory authorities.

Canada: Summary Safety Review: Olanzapine: Assessing the potential risks of syndrome of inappropriate secretion of antidiuretic hormone and hyponatremia

On 31 October 2024, Health Canada announced that it reviewed the potential risks of syndrome of inappropriate secretion of antidiuretic hormone (SIADH) and hyponatremia with the use of olanzapine. The safety review was triggered by a safety report completed by a manufacturer of olanzapine-containing products on the risk of hyponatremia secondary to SIADH, which was prepared following the identification of a published case report during routine surveillance.

Olanzapine is a prescription drug authorized for

sale in Canada for the treatment of schizophrenia and related psychotic disorders, and bipolar disorder. When administered intramuscularly, it may also be used for the rapid control of agitation in these patient populations.

Syndrome of inappropriate secretion of antidiuretic hormone is a condition in which the body makes too much antidiuretic hormone, a hormone that helps regulate the water balance in the body. Too much antidiuretic hormone causes more water to be held in the body and commonly leads to hyponatremia, which is low blood sodium levels.

Symptoms of hyponatremia include muscle cramps, tremor, headache, nausea, and vomiting. If blood sodium levels become too low or if sodium levels drop too quickly, symptoms may progress to seizures, coma and respiratory arrest (absence of breathing), with life-threatening or fatal consequences.

Health Canada reviewed the available information provided by manufacturers, and from searches of the Canada Vigilance database and the scientific literature. Health Canada reviewed 15 cases (1 Canadian and 14 international) of SIADH or hyponatremia in patients taking olanzapine. Twelve of those cases (1 Canadian) reported SIADH and 3 reported hyponatremia only. Of the 15 cases, 13 (11 SIADH [1 Canadian], 2 hyponatremia) were found to be possibly linked to the use of olanzapine and 2 (1 SIADH, 1 hyponatremia) could not be assessed due to missing or contradictory information. Overall, these cases provided limited evidence for a link between the use of olanzapine and the development of SIADH and hyponatremia due to the presence of confounders (other factors that may have contributed to the occurrence of SIADH or hyponatremia) and missing clinical information.

Health Canada also reviewed 30 articles published in the scientific literature that investigated or summarized existing evidence for the association between antipsychotics (including olanzapine) and the development of SIADH and hyponatremia. Due to study limitations, including the presence of confounders, there was limited evidence to support a link between the use of olanzapine and the development of SIADH and hyponatremia.

Health Canada's review could not confirm a definitive link between the use of olanzapine and the development of SIADH and hyponatremia. However, a possible link could not be ruled out.

While a definitive link could not be confirmed, Health Canada's review of the available information could not rule out a possible link between olanzapine and the risks of SIADH and hyponatremia. Despite the limited available evidence, the extensive use of olanzapine in Canada and vulnerability of the patient population who could be prescribed the drug warranted a precautionary approach for these risks. Health Canada will work with the manufacturers to update the CPM for all olanzapine-containing products to include the potential risks of SIADH and hyponatremia.

In Hong Kong, there are 44 registered pharmaceutical products containing olanzapine. All products are prescription-only medicines. As of the end of October 2024, with regard to olanzapine, the Department of Health (DH) had received 25 cases of adverse drug reaction, but these cases were not related to SIADH and hyponatremia. In light of the above Health Canada's announcement, the DH issued letters to inform local healthcare professionals to draw their attention on 1 November 2024, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Batch recall of two products of Apo-Amitriptyline tablets due to presence of impurity

On 18 October 2024, the Department of Health (DH) endorsed a licensed drug wholesaler, Hind Wing Co Ltd, to recall a total of 14 batches of the following two products from the market as a precautionary measure due to the presence of impurity in the products.

Name of product	Hong Kong registration number	Batch number
Apo-Amitriptyline Tablets 10mg	HK-09273	RN6384
		RR0266
		RV1644
		RW8597
		TA6008
		TF8585
		TF8587
		TF8589
Apo-Amitriptyline Tablets 25mg	HK-09274	RM8130
		RR0781
		RV1656
		RW8691
		TA6062
		TF8602

The DH received notification from Hind Wing that the overseas manufacturer of the products is recalling the above batches of Apo-amitriptyline tablets as they exceed or may exceed the accepted level of an impurity, N-Nitrosonortriptyline (NNORT). NNORT is classified as a probable human carcinogen based on results from laboratory tests. As a precautionary measure, Hind Wing is voluntarily recalling the affected batches of products from the market.

The above products, containing amitriptyline, are prescription medicines used for the treatment of depression. According to Hind Wing, the above batches of products had been imported into Hong Kong. The affected batches of products had been supplied to the DH clinics, pharmacies, private doctors, and private hospitals, and re-exported to Macao.

As of the end of 31 October 2024, the DH had not received any adverse reaction reports in connection with the products. A press release was posted in the Drug Office website on 18 October 2024 to alert the public of the product recall. The DH will closely monitor the recall.

Drug Incident

DH urges public not to buy or consume product with undeclared controlled drug ingredient, sildenafil.

On 30 October 2024, the Department of Health (DH) urged the public not to buy or consume a product, namely Firstwell Tongkat Ali Premix Coffee, as it was found to contain an undeclared controlled drug ingredient, namely sildenafil.

Acting upon a public complaint, the DH obtained samples of the above product via online platforms for analysis. Test results from the Government Laboratory revealed that the samples contained sildenafil, which is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138) (the Ordinance). The product is not a registered pharmaceutical product in Hong Kong. The DH's investigation is continuing.

Sildenafil is a prescription drug used for treatment of erectile dysfunction, and should only be used under a doctor's advice and be supplied in a pharmacy under the supervision of a registered pharmacist upon a doctor's prescription. Side effects of sildenafil include low blood pressure, headaches, vomiting, dizziness and transient vision disturbances. It may interact with some drugs (such as nitroglycerin for the treatment of angina) and cause a decrease in blood pressure to dangerous levels. Improper use of sildenafil may pose serious health risks, especially for patients with heart problems.

A press release was posted in the Drug Office website on 30 October 2024 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/

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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.