Drug News
藥 物 情 報

Issue Number 56

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in June 2014 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: Local isolated reports of coring (Engerix-B and Infanrix-IPV+Hib vaccines)

It was noted from the website of Health Sciences Authority (HSA) on 3 June 2014 that GlaxoSmithKline (GSK) in Singapore informed healthcare professionals of the local isolated reports of stopper coring which resulted in the presence of black particles in Engerix-B and Infanrix-IPV+Hib vaccines. Healthcare professionals are advised to observe the instructions within the products' respective package inserts and to visually inspect for particulates before vaccine administration.

In Hong Kong, Engerix-B Paediatric Inj 10mcg/0.5ml (HK-49500), Engerix-B Adult Inj 20mcg/ml (HK-49501), Engerix-B Junior Vaccine Inj 10mcg/0.5ml (HK-54576), Infanrix-IPV+Hib Vaccine (HK-47367), and Infanrix-IPV-Hib Vaccine (DH Pack) (HK-62548) are pharmaceutical products registered by GSK Ltd. All of the above products are prescription only medicines. As confirmed with GSK, the company has not received any complaint on the presence of black particles in Engerix-B and Infanrix-IPV+Hib vaccines within three years. So far, the Department of Health (DH) has not received any adverse drug reaction (ADR) report in connection with black particles in Engerix -B and Infanrix-IPV+Hib vaccines. The DH will keep vigilant on any further update on the captioned issue.

Singapore: The importance of establishing wild-type RAS (exons 2, 3, 4 of KRAS and exons 2, 3, 4 of NRAS) status before treatment with Erbitux® 5mg/ml solution for infusion (cetuximab)

It was noted from the website of HSA on 6 June 2014 that Merck Pte. Ltd. in Singapore informed healthcare professionals of the planned modification to the approved therapeutic indication in metastatic colorectal cancer (mCRC) and updates to the safety information of Erbitux® following a change to the European Union (EU) Summary of Product Characteristics in December 2013. The revised indication for the use of Erbitux® involves a change in the intended patient population to include wild type RAS patients, to mitigate the risk of a negative impact on patients with RAS mutations beyond KRAS exon 2. In addition, healthcare professionals are advised to take into consideration the possibility of infusion-related reactions and to monitor patients closely, especially during the first administration.

In Hong Kong, Erbitux Solution for Infusion 2mg/ml (HK-53330) and 5mg/ml (HK-57484) are pharmaceutical products registered by Merck Pharm (HK) Ltd., and are prescription only medicines. So far, the DH has not received any adverse drug reaction report in relation to infusion of the drug. In view of the HSA's announcement, a letter to healthcare professionals to draw their

attention and urge them to report any ADR related to the drug was issued on 6 June 2014, and the matter will be discussed in the meeting of the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certificate of Clinical Trial/Medicine Test) Committee (the Registration Committee) of the Pharmacy and Poisons Board.

Australia: Investigations into the cause of fevers in children under 5 years for BioCSL Fluvax

On 12 June 2014, the Therapeutic Goods Administration (TGA) had announced that during the 2010 influenza season bioCSL's Fluvax influenza vaccine was associated with a higher rate of fever and fever-related convulsions in children under 5 than other influenza vaccines. The BioCSL researchers found that the likely cause of higher rates of fever and fever-related convulsions was the introduction of new viral strains in that season's vaccine which generated a stronger immune response than seen previously. When processed using the BioCSL standard production method, the new strains also generated certain extra viral components that additionally stimulated the immune system.

The researchers concluded that these factors combined to generate stronger immune responses in a sub-group of the population under 5 years of age that resulted in a higher rate of fever and fever-related convulsions in this group. The TGA has not approved Fluvax for use in children under the age of 5 years. As fevers have been observed in children aged 5 to under 9 years after immunisation with bioCSL Fluvax, health professionals are advised that a decision to vaccinate a child in this age group with the 2014 bioCSL Fluvax vaccine should be based on careful consideration of potential benefits and risks in the individual child.

In Hong Kong, two registered Fluvax products, namely Fluvax Vaccine (HK-42956) and Fluvax Vaccine Inj (Southern Hemisphere) (HK-54227) are registered by Luen Cheong Hong Ltd. (LCH). Both products are prescription only medicines. So far, the DH has not received any adverse drug reaction report in connection with the drugs. As confirmed with LCH, both products are not marketed in Hong Kong since 2010. In view of the TGA's announcement, the matter will be discussed in the meeting of the Registration Committee.

Canada: Zofran® (ondansetron) - dosage and administration of intravenous ondansetron in geriatrics (>65 years of age)

On 12 June 2014, GSK Inc., in consultation with Health Canada, would like to provide healthcare professionals with important new safety information regarding the dosing and administration of intravenous (IV) ondansetron (Zofran®) in geriatrics. New dosing restrictions are recommended to mitigate the risk of QT prolongation in elderly patients (>65 years of age).

In geriatrics, Zofran® is indicated for the prevention of nausea and vomiting associated with emetogenic chemotherapy, including high dose cisplatin, and radiotherapy. There is a risk of dose dependent QT interval prolongation, which is expected to be greater with faster rate of infusion and larger doses for the IV administration. The dosing restrictions for geriatrics are summarized below:

- In patients ≥75 years of age, the initial IV dose must not exceed 8 mg.
- In patients <75 years of age, the initial IV dose must not exceed 16 mg.
- Subsequent IV doses must not exceed 8 mg and may be given 4 and 8 hours after the initial dose.
- All IV doses must be diluted in 50–100 mL of saline or other compatible fluid.
- All IV doses must be infused over no less than 15 minutes.

In Hong Kong, there are 21 registered pharmaceutical products containing ondansetron, seven of which are injectable products. All of them are prescription only medicines. So far, the DH has not received any adverse drug reaction report on QT prolongation in connection with the drug. Safety alerts on IV ondansetron for the use in the elderly had been released by the HSA which had been reported in Drug News Issue No. 50. Letters to inform healthcare professionals to draw their attention on the issue and urge them to report any adverse drug reaction related to the drug were issued on 16 September 2011 and 3 July 2012. The Registration Committee discussed the issue in February 2012 and July 2013, and decided that the sales packs or package inserts of the products should include safety information on risk of QT

prolongation associated with the drug and dose restrictions. For the brand product Zofran Injection, the certificate holder GSK Ltd. has updated the package insert of its IV product Zofran to include the guidance for dosing in geriatrics. In view of Health Canada's announcement, the matter will be discussed in the meeting of the Registration Committee.

US: FDA adding general warning to testosterone products about potential for venous blood clots

On 19 June 2014, the U.S. Food and Drug Administration (FDA) was requiring manufacturers to include a general warning in the drug labeling of all approved testosterone products about the risk of blood clots in the veins. Blood clots in the veins, also known as venous thromboembolism (VTE), include deep vein thrombosis (DVT) and pulmonary embolism (PE). The risk of venous blood clots is already included in the labeling of testosterone products as a possible consequence of polycythemia, an abnormal increase in the number of red blood cells that sometimes occurs with testosterone treatment. As there have been postmarket reports of venous blood clots unrelated to polycythemia, FDA was requiring a change to drug labeling of all testosterone products to provide a more general warning regarding venous blood clots and to ensure this risk is described consistently in the labeling of all approved testosterone products.

Because these clots occur in the veins, this new warning is not related to FDA's ongoing evaluation of the possible risk of stroke, heart attack, and death in patients taking testosterone products.

In Hong Kong, there are eight registered pharmaceutical products containing testosterone which are prescription only medicines. The FDA started investigating the risk of cardiovascular events of testosterone products and the related news was reported in Drug News Issue No. 52. So far, the DH has not received any adverse drug reaction report on venous thromboembolism associated with the use of the drug. In view of the announcement by the FDA, a letter to healthcare professionals to draw their attention and urge them to report any ADR related to the drug was issued on 20 June 2014, and the matter will be discussed in the meeting of the Registration Committee.

US: FDA warns that cancer drug docetaxel may cause symptoms of alcohol intoxication after treatment

On 20 June 2014, FDA was warning that the intravenous chemotherapy drug docetaxel contains ethanol, also known as alcohol, which may cause patients to experience intoxication or feel drunk during and after treatment. We were revising the labels of all docetaxel drug products to warn about this risk. Healthcare professionals should consider the alcohol content of docetaxel when prescribing or administering the drug to patients, particularly in those whom alcohol intake should be avoided or minimized and when using it in conjunction with other medications.

Docetaxel is a prescription chemotherapy drug used to treat different kinds of cancer, including cancers of the breast, prostate, stomach, head and neck cancers, and non-small-cell lung cancer. Several forms of docetaxel are currently marketed, including generics and the brand-name products Taxotere, Docefrez, and Docetaxel Injection. The various products contain different amounts of alcohol, which is used to dissolve the active ingredients so docetaxel can be given intravenously. Healthcare professionals should be aware of the differences in formulations in order to monitor and counsel patients appropriately.

In Hong Kong, there are 25 registered docetaxel-containing pharmaceutical products that contains ethanol and they are prescription only medicines. So far, the DH has not received any adverse drug reaction report in connection with the drug. In view of the announcement by the FDA, a letter to healthcare professionals to draw their attention and urge them to report any ADR related to the drug was issued on 23 June 2014, and the matter will be discussed in the meeting of the Registration Committee. The DH will keep vigilant on any safety update related to the products announced by other drug regulatory authorities.

US: FDA review finds Olmesartan's cardiovascular risks for diabetics not conclusive

On 24 June 2014, FDA had completed its safety review and had found no clear evidence of increased cardiovascular risks associated with use of the blood pressure medication olmesartan in diabetic patients. FDA believes the benefits of

olmesartan in patients with high blood pressure continue to outweigh the potential risks.

FDA safety review was prompted by the results of the ROADMAP trial. The ROADMAP (Randomized Olmesartan and Diabetes Microalbuminuria Prevention) clinical trial examined the effects of olmesartan in patients with type 2 diabetes, to see whether olmesartan could delay kidney damage. There was an unexpected finding of increased risk of cardiovascular death in the olmesartan group compared to the group taking a placebo, or sugar pill. However, the risk of non-fatal heart attack was lower in the olmesartan-treated patients. To evaluate these findings, FDA reviewed additional studies, including a large study in Medicare patients.

Recommendations for use of olmesartan remain the same, but FDA will require information about some of the studies to be included in the drug labels.

In Hong Kong, there are 14 registered pharmaceutical products containing olmesartan and they are prescription only medicines. Related news about the FDA's safety review on the cardiovascular risks of olmesartan was reported in Drug News Issue No. 19. So far, the DH has not received any local adverse drug reaction report of olmesartan. In view of the new FDA's announcement, the matter will be discussed in the meeting of the Registration Committee. The DH will keep vigilant on any safety update related to olmesartan by other drug regulatory authorities.

FDA: FDA warns of rare but serious hypersensitivity reactions with certain over-the-counter topical acne products

On 25 June 2014, FDA was warning that certain over-the-counter (OTC) topical acne products can cause rare but serious and potentially life-threatening allergic reactions or severe irritation. These serious hypersensitivity reactions differ from the local skin irritation that may occur at the product application site, such as redness, burning, dryness, itching, peeling, or slight swelling, that are already included in the Drug Facts labels.

Based on the information reported to FDA, it cannot be determined if the serious hypersensitivity reactions were triggered by the acne products' active ingredients, benzoyl peroxide or salicylic acid, the inactive ingredients, or by a combination of both. FDA was continuing to monitor and evaluate this safety issue, and will work with manufacturers regarding any future label changes that would address the risk of severe hypersensitivity reactions.

In Hong Kong, there are 26 registered pharmaceutical products containing benzoyl peroxide for acne treatment; and 151 registered pharmaceutical products containing salicylic acid for various indications including acne treatment. So far, the DH has not received any local adverse drug reaction report related to topical acne products containing benzoyl peroxide or salicylic acid. In view of the above FDA announcement, the matter will be discussed in the meeting of the Registration Committee. The DH will keep vigilant on any safety update related to topical acne products by other drug regulatory authorities.

US: FDA recommends not using Lidocaine to treat teething pain and requires new Boxed warning

On 26 June 2014, FDA notified health professionals that prescription oral viscous lidocaine 2% solution should not be used to treat infants and children with teething pain. FDA was requiring a Boxed Warning to be added to the prescribing information (label) to highlight this information. Oral viscous lidocaine solution is not approved to treat teething pain, and use in infants and young children can cause serious harm, including death.

Topical pain relievers and medications that are rubbed on the gums are not necessary or even useful because they wash out of the baby's mouth within minutes. When too much viscous lidocaine is given to infants and young children or they accidentally swallow too much, it can result in seizures, severe brain injury, and problems with the heart. Cases of overdose due to wrong dosing or accidental ingestion have resulted in infants and children being hospitalized or dying.

Healthcare professionals should not prescribe or recommend this product for teething pain. FDA is also encouraging parents and caregivers not to use topical medications for teething pain that are available over the counter (OTC) because some of them can be harmful.

In Hong Kong, there are 47 registered

pharmaceutical products containing lidocaine (or lignocaine) for topical oral applications. So far, the DH has not received any local adverse drug reaction report related to these products. In view of the above FDA's announcement, a letter to healthcare professionals to draw their attention and urge them to report any ADR related to the drug was issued on 27 June 2014, and the matter will be discussed in the meeting of the Registration Committee. The DH will keep vigilant on any safety update related to lignocaine for topical oral applications by other drug regulatory authorities.

Drug Recall

Recall of Muro 128 Eye Ointment 5% (HK-58397)

On 11 June 2014, the DH endorsed a licensed drug wholesaler, Bausch & Lomb (HK) Ltd. (Bausch & Lomb), to conduct a voluntary recall of two batches (batch numbers: 151221 and 166592) of Muro 128 Eye Ointment 5% [3.5g per box] from the market due to a quality issue. Muro 128 Eye Ointment 5%, containing sodium chloride, is an over-the-counter medicine used in the eye for temporary relief of swelling symptoms caused by fluid accumulation in the corneal stroma.

The DH received notification from Bausch & Lomb that the product's manufacturer in USA, Bausch & Lomb Incorporated, had found some crystal precipitates in Muro 128 Eye Ointment. The manufacturer's investigation confirmed no anomalies or discrepancies during the manufacturing process and all chemical in process and release testing for all product lots were within specifications. The crystal precipitates may be due to the exposure of product to lower than expected temperature during transit or storage. Bausch & Lomb Incorporated initiated a voluntary recall of 22 affected batches of the product in co-ordination with the US FDA to the retail level. The potential risk of using the affected product includes ocular or corneal damage.

According to Bausch & Lomb, only two of the affected batches (batch numbers: 151221 and 166592), with 1152 boxes in total, had ever been imported to Hong Kong since May 2012. They were all supplied to local private doctors, a private hospital and pharmacies. The DH will closely monitor the recall. As on 11 June 2014, the DH had not received any adverse reaction report related to the use of the product. A notice was released on the Drug Office's website on the same day to alert the public of the recall.

Healthcare providers should stop supplying the affected product to their clients. Members of the public who are consuming the product should consult their healthcare professionals if in doubt.

Total Recall of Ferto Tablets 50mg with pack size of 20 tablets and 30 tablets

On 18 June 2014, the DH instructed a licensed drug wholesaler, Medihealth Pharmaceutical Ltd. (Medihealth), to recall all batches of Ferto Tablet 50mg (Ferto Tablet) with pack size of 20's and 30's from the market because both pack size were not approved. Ferto Tablet is manufactured in India by Arbro Pharmaceuticals Ltd. It contains clomiphene and is a prescription only medicine indicated for the treatment of infertility due to ovulatory failure. It can only be sold at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription.

In Hong Kong, only Ferto Tablet 50mg (HK-59686) with pack size of 100's has been registered.

Through DH surveillance programme, it was found that Medihealth had been distributing Ferto Tablet (pack size of 20's and 30's) to local pharmacies. As neither of the pack size is an approved pack size, it rendered the products unregistered pharmaceutical products.

According to Medihealth, about 2100 and 1300 boxes of Ferto Tablet with pack size 20's and 30's have been supplied to local pharmacies respectively since June 2011. The DH will closely monitor the recall. As on 18 June 2014, the DH had not received any adverse reaction report related to the use of the product. A notice was released on the Drug Office's website on the same day to alert the public of the recall.

People should consult healthcare professionals for advice if feeling unwell or in doubt after consumption.

Girl arrested for suspected illegal sale of unlabelled slimming products with controlled drug ingredients

On 7 June 2014, a joint operation was conducted by the DH and the Police resulting in the arrest of a 15 -year-old girl for suspected illegal sale of Part I poisons and unregistered pharmaceutical products. The products sold were unlabelled slimming products suspected to contain controlled drug ingredients.

Upon DH's investigation of a public complaint previously, samples of products claimed for slimming purpose were purchased for analysis from a seller through communication over a mobile phone application. Test results showed that the products contained western medicines, namely hydrochlorothiazide and fluoxetine respectively. The seller alleged that the slimming products were obtained from Thailand.

Hydrochlorothiazide is a diuretic used for the treatment of hypertension and it may cause hypotension and electrolyte imbalance. Fluoxetine is used for depression and may cause hallucination and insomnia. Hydrochlorothiazide and fluoxetine are both Part I poisons that should only be supplied at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription.

Weight control should be achieved through a balanced diet and appropriate exercise. The public should consult healthcare professionals before using any medication for weight control.

Members of the public are strongly urged not to buy or consume slimming products of unknown or doubtful composition or from unknown sources. Those who have purchased such products should stop taking them immediately and consult healthcare professionals if they are in doubt or feeling unwell.

Public urged not to buy or consume slimming product with undeclared and banned Western drug ingredient

On 11 June 2014, the DH appealed to members of the public not to buy or consume a slimming product called "Lypolysis II" as it is suspected to contain an undeclared and banned drug ingredient that might be dangerous to health.

The appeal followed the DH's receipt of notification from the Hospital Authority (HA) regarding a 22-year-old female patient who was hospitalized for having repeated vomiting. It was found that she had a history of consuming the above slimming product. According to the HA, a sample of the product provided by the patient was found to contain the Part I poison sibutramine.

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

Members of the public who have purchased the above product should stop consuming it immediately. They should consult healthcare professionals for advice if feeling unwell or in doubt after consuming it.

Weight control should be achieved through a balanced diet and appropriate exercise. The public should consult healthcare professionals before using any medication for weight control.

Public urged not to buy or use slimming products labelled as containing drug ingredient yohimbine

On 16 June 2014, the DH appealed to members of the public not to buy or use three oral slimming products namely "Rapidcuts", "Lipo 6" and "Lipo 6 Black" as they were labelled as containing a drug ingredient, yohimbine, which might be dangerous to health.

The appeal followed the DH's investigation upon the receipt of notification of a case from the HA regarding a 29-year-old female patient who was hospitalized for having palpitation, hand tremor, dizziness and anxiety feeling. It was found that she had a history of consuming the above slimming product, "Rapidcuts", which was purchased locally. According to the HA, a sample of the product provided by the patient was found to contain yohimbine.

Yohimbine is a Part I poison and has an antidiuretic effect. Its side-effects include increase in heart rate and blood pressure, anxiety, manic reactions and bronchospasm. Products containing yohimbine can only be sold in a pharmacy under the supervision of a registered pharmacist.

Subsequent to the investigation, related retail shops were raided in a joint operation by the DH and the Police. During the operation, the above three kinds of oral slimming products were seized in two retail shops located in Kowloon Bay and Sheung Wan respectively. A woman aged 23 was arrested by the Police for suspected illegal sale and possession of Part I poison and unregistered pharmaceutical products. Preliminary investigation has so far revealed that the products were sourced outside Hong Kong and no Hong Kong pharmaceutical product registration number was found on the product labels.

Members of the public who have purchased the above products should stop consuming them immediately. They should consult healthcare professionals for advice if feeling unwell or in doubt after consumption.

Weight control should be achieved through a balanced diet and appropriate exercise. The public should consult healthcare professionals before using any medication for weight control.

Retail shop raided for suspected illegal possession of unregistered pharmaceutical products with controlled drug ingredients

On 24 June 2014, a joint operation was conducted by the DH and the Police against a retail shop in Kwun Tong resulting in the arrest of a 39-year-old female for suspected illegal possession of unregistered pharmaceutical products and Part I poison.

Acting upon intelligence, the DH found two suspected unregistered pharmaceutical products being displayed for sale by the retail shop. The two products were called "Baby Teething Gel", containing a Part I poison benzocaine, and "Triple Flex Caplets", containing glucosamine. Hong Kong pharmaceutical product registration numbers were not found on any of the product labels.

Benzocaine is a local anaesthetic for the relief of pain and itching. It may cause side effects such as hypersensitive reactions and methemoglobinemia. The product should only be sold at pharmacies under the supervision of registered pharmacists. Glucosamine is an over-the-counter medicine used for joint problems.

Members of the public should not self-medicate without seeking advice from healthcare professionals. People who have purchased the above products should stop using the products.

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 I poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part I 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.

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.

Velcade for Injection – Risk of possible broken / cracked vials

On 23 June 2014, Johnson & Johnson (HK) Ltd. (J&J), a licensed drug wholesaler, informed the DH of two complaints received from customers relating to cracked / broken Velcade vials. One complaint was received from Germany while another was received from the USA. Upon further inspection during their internal secondary packaging process, prior to release of product to the market, four additional broken / cracked vials were detected.

Healthcare providers are warned of the following potential risk to the patients and personnel handling broken / cracked Velcade vials during dispensing or preparation of the product:

Failure of sterility: a cracked vial may affect the integrity of the vial leading to loss of sterility. Infusion of the non-sterile injection can lead to an increased chance of potential infections, which could be life threatening.

Glass particulate in the vial: cracked or broken Velcade vials may also result in glass particulates in the vial that could potentially lead to the occurrence of thromboembolic events, which potentially could be life threatening.

Accidental exposure: a broken vial can easily be detected and discarded. Broken vials may lead to accidental exposure of the drug to personnel handling the vials. This accidental exposure may result in injuries which could be life threatening.

J&J further added that review of its adverse event surveillance system did not reveal any cases of cracked / broken vial incidents. However, given the nature of these reports and potential risk to patient, J&J recommends that healthcare providers take the following actions when dispensing/ preparing Velcade injection:

- Always wear protective gloves / eye protection / face protection and personal protective equipment.

- Thoroughly inspect the vial for any crack or other damages.

- If a broken / compromised vial is found, do not use it for patient administration.

- If swallowed accidentally, immediately call a poison centre or doctor / physician, as they may potentially result in a fatal outcome.

In Hong Kong, Velcade for Inj 3.5mg (France) (HK -60429), Velcade for Inj 1mg (HK-58055) and Velcade for Inj 3.5mg (HK-53329) containing bortezomib are pharmaceutical products registered by J&J, and they are prescription only medicines. So far, the DH has not received any adverse reaction report in relation to cracked or broken Velcade vials. As confirmed with J&J, only Velcade for Inj 3.5mg (France) (HK-60429) is marketed in Hong Kong and is mainly distributed to HA. As it is an essential medicine and there is no other registered alternative with the same ingredient in local market, healthcare professionals are reminded to consider the use of the medication with thorough inspection for any crack or other damages of the vial when the benefits to the patients outweigh the potential risk. The DH will keep vigilant against the captioned issue and actions taken by other overseas regulatory authorities for consideration of any action deemed necessary.

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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.