Drug News
藥 物 情 報

Issue Number 131

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in September 2020 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

US: FDA alerts healthcare professionals and oncology clinical investigators about efficacy and potential safety concerns with atezolizumab in combination with paclitaxel for treatment of breast cancer

On 8 September 2020, the United States (US) Food and Drug Administration (FDA) announced that it is alerting healthcare professionals, oncology clinical investigators, and patients that a clinical trial studying the use of atezolizumab (Tecentriq) and paclitaxel in patients with previously untreated inoperable locally advanced or metastatic triple negative breast cancer (mTNBC) showed the drug combination did not work to treat the disease.

Atezolizumab in combination with paclitaxel is not approved for use in breast cancer. However, atezolizumab in combination with paclitaxel protein-bound (Abraxane) – a different combination therapy – is currently approved for the treatment of adult patients with mTNBC whose tumors express PD-L1 (PD-L1 stained tumor-infiltrating immune cells of any intensity covering ≥ 1% of the tumor area), as determined by an FDA-approved test. Continued approval of atezolizumab in combination with paclitaxel protein-bound may be contingent on proven benefit of the treatment in additional trials.

Healthcare professionals should not replace paclitaxel protein-bound (Abraxane) with paclitaxel in clinical practice.

The trial, IMpassion131, was a phase 3, multicenter, randomized, double-blind, placebo-controlled trial of atezolizumab in combination with paclitaxel compared with placebo and paclitaxel for patients with mTNBC. In this clinical trial, treatment with atezolizumab and paclitaxel did not significantly reduce the risk of cancer progression and death compared with placebo and paclitaxel in the PD-L1-positive population. Additionally, interim overall survival results favored paclitaxel + placebo, over paclitaxel + atezolizumab in both the PD-L1-positive population and total population.

The FDA will review the findings of IMpassion131 and will communicate new information regarding the IMpassion131 results and any potential changes to prescribing information. The FDA is also evaluating the use of atezolizumab and paclitaxel in ongoing clinical trials for breast cancer and will recommend additional changes as appropriate.

Patients taking atezolizumab and paclitaxel for other approved uses should continue to take their medication as directed by their healthcare professional.

In Hong Kong, Tecentriq Concentrate for Solution for Infusion 1200mg/20ml (HK-65567), Tecentriq Concentrate for Solution for Infusion 1200mg/20ml (HK-66341) and Tecentriq Concentrate for Solution for Infusion 840mg/14ml (HK-66613) are pharmaceutical products containing atezolizumab. All products are registered by Roche Hong Kong Limited, and are prescription-only medicines. As on 5 October 2020, the Department of Health (DH) has received 72 cases of adverse drug reaction (ADR) related to atezolizumab.

In Hong Kong, Tecentriq Concentrate for Solution for Infusion 840mg/14ml (HK-66613) is currently approved in combination with nab-paclitaxel for the treatment of breast cancer. As the FDA's review is ongoing, the DH will remain vigilant on safety update of the drugs issued by the FDA and other overseas drug regulatory authorities.

US: FDA warns website operators illegally selling opioids to consumers

On 10 September 2020, the US FDA announced that it has issued warning letters to 17 website operators for illegally selling unapproved and misbranded opioids online in violation of the Federal Food, Drug, and Cosmetic Act. Misbranded opioids include those offered for sale without a prescription, as well as opioids that lack adequate directions for use.

The affected products include:

- Tramadol 225 mg tablets manufactured by Royal Inc
- Tramal-SR
- Tramadol manufactured by Dimedics
- Tramal
- OL-TRAM
- TOP DOL
- TRAMADOL-X 225
- Tramapar
- Tramadol (Ultram) manufactured by Pharma Chemie co
- Tramadolo HCl
- TAMOL-XX
- Nalbin
- Roxycodone
- OxyNorm
- Tramadol 50 mg/ml manufactured by sicomed

The opioids offered for sale include products such as tramadol and oxycodone. These are prescription drugs that have significant risks of addiction, abuse and misuse, which can lead to overdose and death, and should only be used under the supervision of a licensed healthcare provider. In addition to the significant risks of addiction, abuse and misuse, opioids can cause life-threatening respiratory depression (breathing problems), which can lead to overdose and death, and withdrawal symptoms in newborn babies. When taken with other central nervous system depressants, including alcohol, the use of opioids may result in coma or death.

In Hong Kong, there are 6 oxycodone-containing pharmaceutical products with brand name "Oxynorm", namely Oxynorm Cap 20mg (HK-59575), Oxynorm Cap 5mg (HK-59576), Oxynorm Cap 10mg (HK-59577), Oxynorm Solution for Injection or Infusion 10mg/ml (HK-61835), Oxynorm Concentrate Oral Solution 10mg/ml (HK-66357) and Oxynorm Liquid Oral Solution 5mg/5ml (HK-66358). All products are registered by Mundipharma (Hong Kong) Limited, and are prescription-only medicines. The other products mentioned in the above FDA's announcement are not registered pharmaceutical products.

For retail sale of prescription-only medicines, they should be sold in the Authorized Seller of Poisons (i.e. pharmacy) under the supervision of the registered pharmacist upon the doctor's prescription. Members of the public should not buy or consume products of doubtful composition or from unknown sources. They should consult healthcare professionals if they are in doubt or feeling unwell.

EU: Prevymis (letermovir) concentrate for solution for infusion - Essential to administer through sterile 0.2 micron or 0.22 micron polyethersulfone (PES) in-line filter

On 11 September 2020, the European Medicines Agency (EMA) of the European Union (EU) announced that a Direct Healthcare Professional Communication was issued to inform healthcare professional on the following important prescribing information:

- The diluted solution of Prevymis (letermovir concentrate for solution for infusion 20 mg/mL) MUST be infused through a sterile 0.2-micron or 0.22-micron PES inline filter.
- Inspect the vial contents for discoloration and particulate matter. The concentrate is a clear and colorless solution and may contain a few product-related small translucent or white particles. Once diluted, the solution for infusion is clear and ranges from colorless to yellow.
- Do not use if the concentrate or diluted solution is cloudy, discolored, or contains matter other than a few small translucent or white particles.
- Do not use Prevymis concentrate for solution for infusion with intravenous (IV) bags and infusion set materials containing polyurethane or diethylhexyl phthalate (DEHP). Materials that are phthalate-free are also DEHP-free.

Prevymis concentrate for solution for infusion may contain product-related small translucent or white particles. Use of a sterile 0.2-micron or 0.22-micron PES in-line filter prevents possible administration of particles that have been seen in vials of Prevymis injection. Administration through a sterile 0.2-micron or 0.22-micron PES in-line filter has no impact on Prevymis dosage.

Administration of Prevymis diluted solution always requires the use of a sterile 0.2 micron or 0.22 micron PES in-line filter, regardless of whether these product-related particles are visible in the vial or diluted solution.

The healthcare professionals who may be involved in the reconstitution and administration of Prevymis are advised to carefully follow the reconstitution and administration instructions in the Summary(ies) of Product Characteristics (SmPC) and the package leaflet (PIL) for Prevymis, as summarized below:

- Prevymis must be diluted prior to IV use according to the instructions in the SmPC.
- Inspect the vial contents for discoloration and particulate matter prior to dilution. Prevymis concentrate for solution for infusion is a clear and colorless solution and may contain a few product-related small translucent or white particles.
- Do not use the vial if the solution is cloudy, discolored, or contains matter other than a few small translucent or white particles.
- Do not use Prevymis concentrate for solution for infusion with IV bags and infusion set materials containing polyurethane or the plasticizer DEHP. Materials that are phthalate-free are also DEHP-free.
- Once diluted, the solution of Prevymis is clear and ranges from colorless to yellow. Variations of color within this range do not affect the quality of the product.
- Discard the diluted solution if the solution is cloudy, discolored, or contains matter other than a few small translucent or white particles.
- The diluted solution must be administered through a sterile 0.2-micron or 0.22- micron PES in-line filter.

Prevymis is indicated for prophylaxis of cytomegalovirus (CMV) reactivation and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant. Prevymis may be administered orally, with Prevymis 240 mg or 480 mg tablets, or intravenously, using Prevymis concentrate for solution for infusion after suitable dilution.

In Hong Kong, Prevymis Concentrate for Solution for Infusion 480mg/24ml (HK-66122) and Prevymis Concentrate for Solution for Infusion 240mg/12ml (HK-66125) are pharmaceutical products registered by Merck Sharp & Dohme (Asia) Ltd (MSD), and are prescription-only medicines. As confirmed with MSD, an application for change of the package insert that encompasses the above precautions has already been submitted to the DH; and the application has been under evaluation. In view of the EMA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 14 September 2020. The DH will remain vigilant on any safety update issued by overseas drug regulatory authorities.

Canada: ESBRIET (pirfenidone) and the risk of drug-induced liver injury

On 14 September 2020, Health Canada announced that drug-induced liver injury (DILI) in the form of transient and clinically silent elevations in transaminases has been commonly reported in patients treated with ESBRIET (pirfenidone). Rare DILI cases have been associated with serious clinical consequences including isolated cases with fatal outcome.

Serious hepatic adverse events including isolated cases with fatal outcome have recently been reported in the post-market setting in idiopathic pulmonary fibrosis (IPF) patients treated with ESBRIET. The majority of the reported hepatic events occurred within the first 6 months of treatment. No alternative etiologies or confounding factors could be found in these reports, which were therefore deemed clinically relevant cases of DILI. In the absence of a plausible pharmacodynamic mechanism, these cases appear possibly triggered by idiosyncratic reactions to pirfenidone.

Information for consumers:

- ESBRIET is a prescription medicine used to treat IPF in adults. IPF is a condition in which the tissue in the lungs becomes scarred over time, making it difficult to breathe.
- In some patients, ESBRIET has been associated with DILI, which can be serious and life-threatening.
- Before taking ESBRIET, patients should talk to their healthcare professional if they have, or have had, liver problems. ESBRIET may cause liver problems and other abnormal blood test results. Patients with severe or end-stage liver disease should not use ESBRIET. ESBRIET should be used with caution and careful monitoring in patients with mild or moderate liver issues. Before and during treatment, patients should have blood tests done to check their liver function.

- If patients experience signs of liver injury such as, tiredness, yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, or loss of appetite, they need to stop taking ESBRIET and seek immediate medical attention.

Healthcare professionals are advised to:

- Perform liver function tests (alanine aminotransferase, aspartate aminotransferase, and bilirubin) before initiating treatment with ESBRIET, subsequently at monthly intervals for the first 6 months, and then every 3 months thereafter.
- Promptly measure liver function tests in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice.
- Consider discontinuation or dose adjustments in the event of liver enzyme elevation.
- Not use ESBRIET in patients with severe hepatic impairment or end-stage liver disease.
- Use ESBRIET with caution in patients with pre-existing mild to moderate hepatic impairment (Child-Pugh Class A and B).

The Canadian Product Monograph for ESBRIET has been updated to include this new safety information.

In Hong Kong, Esbriet Capsules 267mg (HK-64288) is a registered pharmaceutical product containing pirfenidone. The product is registered by Roche Hong Kong Limited, and is a prescription-only medicine. As on 5 October 2020, the DH has received one case of ADR related to pirfenidone, but this case is not related to liver injury. Related news was previously issued by Singapore Health Sciences Authority (HSA), and was reported in the Drug News Issue No. 122. The DH issued a letter to inform local healthcare professionals to draw their attention on 19 December 2019. In light of the above Health Canada's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board (Registration Committee).

Singapore: Temporary suspension of sales of Esmya (ulipristal acetate) tablet 5 mg

On 17 September 2020, the HSA informed healthcare professionals about the temporary suspension of the sales of Esmya (ulipristal acetate) tablet 5 mg, used for the treatment of symptoms of uterine fibroids. The sales of Esmya has been temporarily suspended in Singapore since March 2020 as a precautionary measure, while the HSA conducts a reassessment on the benefit-risk profile of Esmya. This was due to ongoing concerns of its association with liver injury, including overseas reports of serious liver injury resulting in liver transplantations that were surfaced by the EMA.

In 2018, the EMA had conducted a safety review on the risk of serious liver injury with Esmya, which concluded that there was a risk of rare but serious liver injury with the product. As a result, additional measures, such as contraindicating the use of Esmya in patients with underlying liver disorders, more frequent liver function monitoring and restricting the use of multiple courses of the product in women who are not eligible for surgery, were put in place to manage this risk. As a new case of serious liver injury resulting in liver transplantation had occurred despite these measures, the EMA restarted a review in March 2020, to determine if the previous risk minimisation measures were adequate to manage this safety concern.

The EMA's review was restricted only to ulipristal acetate 5 mg for the treatment of symptoms of uterine fibroids and did not affect the use of ulipristal acetate 30 mg as a single-dose medicine for emergency contraception, as there was no concern about liver injury with the latter. In September 2020, the EMA completed its review of this safety concern, and recommended the revocation of the marketing authorisation of all ulipristal acetate 5 mg products, including Esmya. The EMA's review took into consideration the reported cases of serious liver injury, as well as the inputs of patient and healthcare professional representatives, including experts in gynaecology. As it was not possible to identify which patients were most at risk of liver injury, or the measures which could reduce this risk, the EMA concluded that the risks of using ulipristal acetate 5 mg for the treatment of symptoms of uterine fibroids outweighed their benefits. Therefore, the EMA recommended that these products should no longer be marketed in the EU.

Since 2017, the HSA has been closely monitoring the overseas reports of rare but serious liver injuries associated with Esmya. In 2018, the HSA conducted a benefit-risk assessment on the risk of

rare but serious liver injury associated with the use of Esmya in the treatment of uterine fibroids. It was assessed that the benefits of Esmya continue to outweigh the risks of serious liver injury (approximately 1 in 95,000 patients) for its locally approved use, with the implementation of additional risk mitigation measures. These measures include: a) contraindicating the use in patients with underlying liver disorders, b) restricting the use of multiple treatment courses in women who are not eligible for surgical treatment and, c) increasing the frequency of liver function monitoring. These measures were communicated to healthcare professionals via the company's Dear Healthcare Professional Letter in April 2019 and a publication in the September 2019 issue of the HSA ADR News Bulletin. A patient information brochure was also developed and disseminated by the company, to advise patients on the potential risk of serious liver injury and the signs and symptoms to look out for, during treatment with Esmya. As on 17 September 2020, the HSA has not received any ADR reports of serious liver injury, or liver failure, associated with Esmya treatment in Singapore.

Following the notification of an overseas case report of serious liver injury with Esmya leading to liver transplantation despite the implementation of risk minimisation measures, the HSA has worked with the company to implement the temporary suspension of the sales of Esmya in March 2020 as a precautionary measure, while the HSA reassesses the benefit versus risk profile of the product. In the interim, the HSA has also issued an advisory for healthcare professionals, including assessing if a switch to alternative therapies was appropriate for their patients, monitoring the liver function of patients who have been prescribed Esmya, and not to start new patients on Esmya.

The HSA's reassessment of the benefit-risk profile of Esmya is currently ongoing, and the review will take into consideration the latest information from overseas developments. The HSA will keep healthcare professionals updated on the outcomes of the review when completed.

In Hong Kong, Esmya (ulipristal acetate) Tablets 5mg (HK-62553) is a pharmaceutical product registered by Orient Europharma Co. Ltd, and is a prescription-only medicine. As on 5 October 2020, the DH has not received any case of ADR related to Esmya.

Related news on the previous review of Esmya was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 98, 100, 103, 106 and 114. The DH issued a letter to inform local healthcare professionals to draw their attention on the risk of serious liver injury on 12 February 2018. In December 2018, the Registration Committee discussed the matter, and decided that the sales pack or package insert of the product should include the relevant safety information.

Related news on the recent review of Esmya was previously issued by various overseas drug regulatory authorities, and was reported in the Drug News Issue No. 125. The DH issued a letter to inform local healthcare professionals to draw their attention on the EMA's recommendation to suspend ulipristal acetate for uterine fibroids during ongoing review of liver injury on 16 March 2020.

On 20 March 2020, the DH endorsed Orient Europharma Co. Ltd to voluntarily recall Esmya Tablets 5mg (HK-62553) from patients due to the potential risk of liver injury. The recall was reported in the Drug News Issue No. 125 and has been completed.

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

UK: Transdermal fentanyl patches for non-cancer pain: do not use in opioid-naive patients

On 23 September 2020, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) announced that the Commission on Human Medicines (CHM) has recommended that fentanyl transdermal patches are contraindicated in opioid-naive patients in the UK, following a review of the risks associated with use of opioid medicines for non-cancer pain.

Considerable concern has been raised regarding the prescribing of opioids in the UK. In 2019, the CHM convened an Expert Working Group to examine the benefits and risks of opioids in the relief of non-cancer pain. During this review it was noted that there have been reports of serious harm, including fatalities, associated with fentanyl patches in both opioid-naive patients and opioid-experienced patients. Up to May 2020, the MHRA has received 13 Yellow Card reports in which opioid-naive patients have experienced

respiratory depression following use of fentanyl and additional Yellow Card reports in which respiratory depression was reported in patients switched from another opioid to an inappropriately high dose of fentanyl. There was no evidence of intentional overdose in these cases.

There is considerable risk of respiratory depression with the use of fentanyl especially in opioid-naive patients. There is also significant risk with too rapid an escalation of dose, even in long-term opioid users.

Fentanyl is a potent opioid analgesic, a 12 microgram (µg) per hour fentanyl patch equates to daily doses of oral morphine of up to 45mg a day. Because of the risk of significant respiratory depression, in non-cancer patients fentanyl patches should only be used in those who have previously tolerated opioids. The CHM has recommended a strengthening of the current warnings and a contraindication for use in opioid-naive patients in the UK for non-cancer pain.

The initial dose of fentanyl should be based on a patient's opioid history. Please consult the SmPC for each medicine for information on starting doses and dose conversion. Prescribers should take into account the morphine equivalence of fentanyl.

Advice for healthcare professionals:

- Fentanyl is a potent opioid, a 12 µg per hour fentanyl patch equates to daily doses of oral morphine of up to 45mg a day.
- Do not use fentanyl patches in opioid-naive patients.
- Use other analgesics and other opioid medicines (opioids) for non-cancer pain before prescribing fentanyl patches.
- If prescribing fentanyl patches, remind patients of the importance of: not exceeding the prescribed dose; following the correct frequency of patch application, avoiding touching the adhesive side of patches, and washing hands after application; not cutting patches and avoiding exposure of patches to heat including via hot water (bath, shower); ensuring that old patches are removed before applying a new one; and following instructions for safe storage and properly disposing of used patches or patches that are not needed, it is particularly important to keep patches out of sight and reach of children at all times.
- Make patients and caregivers aware of the signs and symptoms of fentanyl overdose and advise them to seek medical attention immediately if overdose is suspected.
- Remind patients that long-term use of opioids in non-cancer pain (longer than 3 months) carries an increased risk of dependence and addiction, even at therapeutic doses; before starting treatment with opioids, agree with the patient a treatment strategy and plan for end of treatment.

In Hong Kong, there are 4 registered pharmaceutical products which are transdermal patch containing fentanyl, namely Durogesic Transdermal Patch 12mcg/h (HK-53883), Durogesic Transdermal Patch 25mcg/h (HK-53755), Durogesic Transdermal Patch 50mcg/h (HK-53753) and Durogesic Transdermal Patch 100mcg/h (HK-53754). All products are registered by Johnson & Johnson (Hong Kong) Ltd, and are prescription-only medicines. As on 5 October 2020, the DH has received one case of ADR related to fentanyl, but this case is not related to respiratory depression. In light of the above MHRA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 24 September 2020, and the matter will be discussed by the Registration Committee.

UK: Insulins (all types): risk of cutaneous amyloidosis at injection site

On 23 September 2020, the MHRA announced that cutaneous amyloidosis at the injection site has been reported in patients using insulin and this may affect glycaemic control.

A recent European review of reports of insulin-derived cutaneous amyloidosis at insulin injection sites concluded that there is a clear causal relationship between cutaneous amyloidosis and all insulins and insulin-containing products. The SmPC and Patient Information Leaflets for all insulins and insulin-containing products in the UK are being updated to include this risk. Advice will also make clear the importance of site rotation and careful blood glucose monitoring following change of injection site to an unaffected area.

Insulin-derived amyloidosis is a specific form of localised cutaneous amyloidosis composed of insulin fibrils. It is likely caused by insulin accumulation at the injection sites, especially if these sites are used for repeated subcutaneous injections.

The European review considered cases of insulin-derived cutaneous amyloidosis reported in patients treated with all types of insulin. Some were identified by either histological examination, computerised tomography, or a combination of these. Presence of insulin in the amyloid was recognised by immunohistochemical analysis and in a single case further validated by mass spectrometry. In many of the cases initially analysed of the review, this resulted in poor glycaemic control (hyperglycaemia and hypoglycaemia).

The evidence showed in many cases patients were routinely injecting into the same sites repeatedly rather than rotating injection sites. When outcome of glycaemic control was reported, most patients recovered after they began to use a proper site-rotation technique.

In the UK, up until the end of July 2019, 2 reports of cutaneous amyloidosis in patients receiving insulin therapy have been received via the MHRA's Yellow Card Scheme. The European review was not able to estimate the frequency of cutaneous amyloidosis in patients using insulin from the data available, but reports have been received only very rarely. The literature suggests that cases of cutaneous amyloidosis may be under-reported and misdiagnosed as lipohypertrophy (a common increase in fat cells due to growth factor effect of insulin). Both conditions are characterised by lumps in the skin. However, where lipohypertrophy lesions are lobular and regress after stopping insulin injection, amyloid lesions are more solid and firm, do not regress quickly, and usually require surgical excision to treat.

While amyloid lesions can delay insulin absorption and affect glycaemic control if used as a site for administration, the skin changes are thought to be localised. Although some cases of cutaneous amyloidosis were reported as of a serious nature, they were mostly reported as such due to hospital admission to resect amyloid lesion. Aside from impact on glycaemic control, no other complications have been recognised.

Patients who inject insulin at the same site regularly are at an increased risk of developing cutaneous amyloidosis at the injection site and consequently may have poor diabetes control due to lack of insulin absorption due to the amyloid mass. To prevent or reduce this, patients should be advised to rotate injection sites within the same body region. There is a risk of hypoglycaemia in patients that suddenly change injection site from an area with cutaneous amyloidosis to an unaffected area (for example, changing the injection site from the torso to the leg). Patients should therefore carefully monitor blood glucose after changing injection site and consider adjusting the dose of insulin or antidiabetic medication to avoid hypoglycaemia, as needed.

Advice for healthcare professionals:

- Injection of insulin (all types) can lead to deposits of amyloid protein under the skin (cutaneous amyloidosis) at the injection site.
- Cutaneous amyloidosis interferes with insulin absorption, and administration of insulin at an affected site can affect glycaemic control.
- Remind patients to rotate injection sites within the same body region to reduce or prevent the risk of cutaneous amyloidosis and other skin reactions (for example, lipodystrophy).
- Consider cutaneous amyloidosis as a differential diagnosis to lipodystrophy when a patient presents with subcutaneous lumps at an insulin injection site.
- Advise patients that insulin may not work very well if they inject into an affected 'lumpy' area; to contact their doctor if they are currently injecting insulin into a 'lumpy' area before changing injection site since a sudden change may result in hypoglycaemia; to monitor carefully blood glucose after a change in injection site and that dose adjustment of insulin or other antidiabetic medication may be needed.

In Hong Kong, there are 54 registered pharmaceutical products containing insulin. These products are drugs under supervised sales or prescription-only medicines. As on 5 October 2020, the DH has received 85 cases of ADR related to insulin, but these cases are not related to cutaneous amyloidosis. In light of the above MHRA's announcement, the DH issued a letter to inform local healthcare professionals to draw their attention on 24 September 2020, and the matter will be discussed by the Registration Committee.

US: FDA warns about serious problems with high doses of the allergy medicine diphenhydramine (Benadryl)

On 24 September 2020, the US FDA announced that it is warning that taking higher than recommended doses of the common

Safety Update

over-the-counter (OTC) allergy medicine diphenhydramine (Benadryl) can lead to serious heart problems, seizures, coma, or even death. The FDA is aware of news reports of teenagers ending up in emergency rooms or dying after participating in the "Benadryl Challenge" encouraged in videos posted on social media. The FDA is investigating these reports and conducting a review to determine if additional cases have been reported. The FDA will update the public once it has completed its review or has more information to share.

Consumers, parents, and caregivers should store diphenhydramine and all other OTC and prescription medicines up and away and out of children's reach and sight. The FDA recommends they lock up medicines to prevent accidental poisonings by children and misuse by teens. Always read the Drug Facts label included on all OTC medicines to find out if they contain diphenhydramine, how much and how often they should take them, and important safety information. Do not take more than the dose listed on the label, as doing so can cause serious problems.

Healthcare professionals should be aware that the "Benadryl Challenge" is occurring among teens and alert their caregivers about it. Encourage teens and caregivers to read and follow the Drug Facts label. In the event of an overdose, healthcare professionals should attempt to determine whether a patient with a suspected overdose took diphenhydramine.

Diphenhydramine is an antihistamine used to temporarily relieve symptoms due to hay fever, upper respiratory allergies, or the common cold, such as runny nose and sneezing.

In Hong Kong, there are 305 registered pharmaceutical products containing diphenhydramine, of which 57 products are oral preparations. As on 5 October 2020, the DH has received one case of ADR related to diphenhydramine, but this case is not related to overdose. Consumers are advised to check the product label carefully and follow the product instructions accordingly.

Drug Recall

DH endorsed recall of two pharmaceutical products

On 14 September 2020, the DH endorsed a licensed drug wholesaler, Suntol Medical Ltd. (Suntol), to recall Royalsense Acne Gel 1% (HK-48233) and Lysozyme Tablets 90mg (Sinphar) (HK-48153), from the market as a precautionary measure due to a stability issue.

The DH received notification from Suntol that Royalsense Acne Gel 1% and Lysozyme Tablets 90mg (Sinphar) are being recalled in Taiwan, as the content of active ingredients in the products failed to meet the product specifications during a long-term stability study. Though the products would not cause a health harm to users, the issue might affect the efficacy of the products. As a precautionary measure, Suntol is recalling the products in Hong Kong.

Royalsense Acne Gel 1%, containing clindamycin, is a prescription medicine used for the topical treatment of acne. Lysozyme Tablets 90mg (Sinphar), containing lysozyme, is an OTC medicine used as adjunctive treatment for certain inflammatory conditions. According to Suntol, the products have been supplied to local private doctors and pharmacies.

As on 5 October 2020, the DH has not received any adverse reaction reports in connection with the products.

Patients who are using the above products should seek advice from their healthcare professionals for appropriate arrangements. Press release was posted on the Drug Office website on 14 September 2020 to alert the public of the products recall.

Drug Incident

Man arrested for suspected illegal possession of nicotine-containing liquids for e-cigarettes

On 29 September 2020, the DH and the Police conducted a joint operation against the illegal possession of nicotine-containing liquids intended for use with electronic nicotine delivery systems, commonly known as e-cigarettes.

Acting upon a public complaint, the DH raided a

retail store in Sham Shui Po and found a number of brands of liquids for use in e-cigarettes labelled with nicotine contents, including the brands HUANXI, RELX, GENTLE and SECRET.

During the operation, a 24-year-old man was arrested for suspected illegal possession of Part 1 poisons and unregistered pharmaceutical products.

Smokers are advised to quit smoking for their own health and that of others. They are encouraged to make use of smoking cessation services through the DH's Integrated Smoking Cessation Hotline (1833 833). Information on smoking cessation can also be obtained from the DH's Tobacco and Alcohol Control Office website (www.taco.gov.hk).

Press release was posted on the Drug Office website on 30 September 2020 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 $30,000 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: ***Undesirable Medical Advertisements and Adverse Drug Reaction Unit,***
Drug Office, Department of Health,
Suites 2002-05, 20/F, AIA Kowloon Tower,
Landmark East, 100 How Ming Street,
Kwun Tong, Kowloon

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.