Drug News
藥 物 情 報

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This is a monthly digest of local and overseas drug safety news and information released by the Drug Office of the Department of Health in the month as stated above. For the latest news and information, please refer to public announcements or the website of the Drug Office of the Department of Health (http://www.drugoffice.gov.hk).

Safety Update

Australia: Why hasn't the TGA taken Stilnox off the market?

Following the alert issued by Health Canada on November 2011 about the association of Sublinox (zolpidem tartrate) with complex sleeping behaviours, Therapeutic Goods Administrtion (TGA) of Australia on 6 July 2012 stated that Stilnox (zolpidem) was a medicine of value when used properly, particularly for patient with severe insomnia, and should remain available for use in Australia. According to TGA, since 2008, the following warning has been highlighted by a box message in the product information of zolpidem:

> *"Zolpidem may be associated with potentially dangerous complex sleep-related behaviours which may include sleep walking, sleep driving and other bizarre behaviours. Zolpidem is not to be taken with alcohol. Caution is needed with other CNS depressant drugs. Limit use to four weeks maximum under close medical supervision."*

Since then, a decreasing number of related adverse events was received which suggested the effectiveness of the above warning and thus TGA was of the view that there was no specific new safety signal of concern that would require any further action at this time.

In Hong Kong, there are 14 registered pharmaceutical products containing zolpidem. They are all prescription medicines indicated for short term management of insomnia. The warning of "complex sleep-related behaviours" was already a labelling requirement for products containing zolpidem. A letter to healthcare professionals was issued on 6 December 2011. As stated in Issue No. 26 of Drug News, 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 (Registration Committee) of the Pharmacy and Poisons Board.

Canada: Alert of ImmuCyst® [Bacillus Calmette-Guérin (BCG), sub strain Connaught] manufactured in Sanofi Toronto

On 11 July 2012, Health Canada completed a risk assessment of ImmuCyst® produced at Sanofi Pasteur's manufacturing plant in Toronto, and concluded that the product should remain available to bladder cancer patients, provided the drug continues to meet quality assurance standards. The review was initiated when mould was found in the sterile manufacturing areas where ImmuCyst® was produced during an inspection. On 13 July 2012, Health Canada further announced that Sanofi Pasteur had halted the distribution of ImmuCyst® back in April 2012 when they found that the validation of one of the required release tests on sterility failed to demonstrate an acceptable ability to detect mould and yeast. Sanofi Pasteur thus decided to renovate the facility and temporarily suspended the production of BCG. So far, there was no evidence of contamination in currently released lots of ImmuCyst® and no reports of infections that might be caused by contamination of the product in the post marketing adverse event surveillance. In consultation with Health Canada, it had determined that the benefits of the product to bladder cancer patients outweigh the risk of potential microbial contamination.

In Hong Kong, ImmuCyst BCG (HK-37556) is registered by Sanofi-Aventis HK Ltd. (Sanofi) and is a prescription medicine. ImmuCyst is indicated for intravesical use in the treatment and prophylaxis of primary or recurrent carcinoma in situ of the

urinary bladder and for prophylaxis following transurethral resection of primary or recurrent stage T_a and/or T1 papillary tumours or any combination thereof, regardless of antecedent intraversical treatment. Department of Health (DH) had requested Sanofi to provide documentary evidence to prove the quality of the product. Subsequently the Certificates of Analysis of all the available batches in HK were provided, and they indicated there was no microbial growth. Based on risk assessment, DH considered ImmuCyst should remain available to bladder cancer patients as there is no alternative product for this indication in Hong Kong and evidence so far showed that the product had met the required quality standard. A letter to health care professionals was issued on 12 July 2012. DH will keep vigilant against any updated safety and qualtiy issues on the product.

US, Singapore: Glass vials defects of more batches of Hospira injectables

Following the alert of paclitaxel issued by Health Canada as reported in Issue No. 32 of Drug News, the Food Drug Administration (FDA) of US announced on 13 July 2012 that Hospira Inc. conducted a recall of 19 batches of carboplatin, cytarabine, paclitaxel and methotrexate in the US. This was due to visible particles embedded in the glass located at the neck of the vials. There may be potential for the products to come into contact with the embedded particles and the particles may become dislodged into the solution. In the event in which particulate matter could be injected into a patient, there may be the potential for patient injury where medical intervention may be required. So far, Hospira had not received any reports of adverse events related to these lots.

On 16 July 2012, the Health Sciences Authority also announced the recall of 2 batches of Anzatax Injection Concentrate 300mg/50ml (paclitaxel) due to the same reason in Singapore.

In Hong Kong, Methotrexate Inj 50mg/2ml (HK-16293) and 1g/10ml (HK-25273), Fluorouracil Inj 250mg/5ml (HK-16296), Cytarabine Inj 10% (HK-35149), Anzatax Inj 150mg/25ml (HK-40639) and 30mg/5ml (HK-40640), Desferrioxamine Mesylate Inj 500mg (HK-42593), Epirubicin Hydrochloride Inj 2mg/ml (HK-51117), Oxaliplatin for Inj 100mg (HK-55662) and 50mg (HK-55663), Oxaliplatin conc for soln for Infusion 50mg/10ml (HK-57506) and 100mg/20ml (HK-57507) are registered by Hospira Ltd. All are prescription medicines. Desferrioxamine is an anti-dote medicine whereas others are anti-cancer medicines. As confirmed by the company, the affected products had never been imported to Hong Kong. In addition, Hospira Ltd. stated that the vial defect was found in only one batch of glassware (lot number: N110565) which had not been used in any products supplied to Hong Kong. DH will keep vigilant against any updated safety and quality news of the issue.

EU, Canada: Recommendation on limiting the long-term use of calcitonin medicines

On 20 July 2012, the European Medicines Agency (EMA)'s Committee for Medicinal Products for Human Use (CHMP) recommended that calcitonin-containing medicines should only be used for short-term treatment, because of evidence that long-term use of these medicines was associated with an increased risk of cancer. In addition, CHMP recommended withdrawing the intranasal formulation of calcitonin which indicated for the treatment of osteoporosis. As a result, calcitonin would only be available as a solution for injection and infusion, and should only be used for:

- prevention of acute bone loss due to sudden immobilisation, with treatment recommended for two weeks with a maximum duration of four weeks;
- Paget's disease in patients who do not respond to alternative treatments or for whom such treatments are not suitable, with treatment normally limited to three months;
- hypercalcaemia caused by cancer.

In response to this recommendation released by EMA, Health Canada announced on 31 July 2012 that the Authority was currently reviewing all available information to determine any appropriate local action.

In Hong Kong, four calcitonin-containing products are registered, namely, Apo-Calcitonin Nasal Spray 200IU/spray (HK-58746), Miacalcic Nasal Spray 200IU (HK-43614), Miacalcic Inj 100IU/ml (HK-27880) and Miacalcic Inj 50IU/ml (HK-28413). They are prescription medicines. Nasal spray is indicated for osteoporosis, bone pain, Paget's disease and neurodystrophic disorders; apart from these indications, the injectable form is also indicated for hypercalcaemia and acute pancreatitis.

Safety Update

In view of the EMA's recommendation, a letter to healthcare professionals was issued on 23 July 2012 and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board.

Canada: Potential malfunction of the delivery device of Pulmicort Turbuhaler (budesonide) 200 µg per metered dose (200 doses unit)

On 23 July 2012, Health Canada informed healthcare professionals that product complaints for Pulmicort Turbuhaler 200 µg per metered dose (200 doses unit) were received regarding the malfunction of the delivery device that resulted in a failure to dispense the dose of medication. The patient would not hear the 'click' sound when the 'turn grip' was rotated, and the intended dose of medication would not be loaded into the unit. Patients who did not realize that the dose had not been loaded may go for a period of time without receiving the prescribed treatment. Health Canada reminded healthcare professionals the importance to discuss and reinforce the proper use of the Pulmicort Turbuhaler device with patients. Patients were instructed to listen for the 'click' sound, as an indication that the inhaler had been loaded and was ready to use. If a patient believed that their Pulmicort Turbuhaler was not working properly, they should contact their healthcare professionals.

In Hong Kong, Pulmicort Turbuhaler 200µg per metered dose (HK-33965) is registered by AstraZeneca Hong Kong Ltd. (AstraZeneca) and is available in two dosing units, i.e., 100 doses and 200 doses. It is a prescription medicine indicated for the treatment of bronchial asthma. DH requested AstraZeneca to provide the investigation report related to the potential malfunction of the delivery device of the product. A letter to healthcare professionals and press statement were released on 27 July 2012 to alert the healthcare professionals and the public on the issue. Healthcare professionals were reminded to reinforce the proper use of the Pulmicort Turbuhaler device with patients (Turn, Click, Inhale) and remind their patients the importance of listening to the 'click' sound. The investigation revealed that the cause was due to a partially broken/damaged tooth in the dosing unit and the cavity mould was found to be in compliance with the measurements specified in the tool drawings. AstraZeneca also confirmed that the defect only confined to Pulmicort Turbuhaler 200µg per metered dose (200 doses unit). Based on risk assessment, DH instructed AstraZeneca to quarantine the remaining stock of Pulmicort Turbuhaler 200µg per metered dose (200 doses unit) and allowed to distribute the product unless with good quality delivery device. DH will keep vigilant against any updated safety and quality issue of the product.

Drug Recall

Batch recall of Apo-Trifluoperazine Tablet 5mg (HK-09272)

On 25 July 2012, DH endorsed a licensed drug wholesaler, Hind Wing Co Ltd (Hind Wing), to recall from market two batches of Apo-Trifluoperazine Tablet 5mg (lot numbers: JW2265 and JW2266) on quality grounds. Apo-Trifluoperazine Tablet 5mg is a tranquilliser and is a prescription medicine which can only be sold with doctor's prescription and under the supervision of pharmacists at registered pharmacies.

The recall was initiated because the product's Canadian manufacturer, Apotex Inc, found that the assay result was outside the specification during the post-marketing stability study. According to Hind Wing, only two of the affected batches had been imported into Hong Kong. The active ingredient of batches JW2265 and JW2266 was found to be 91.7% and 92.0% of the label's claim respectively while the specification should be 92.5% to 107.5%.

The two affected batches were imported into Hong Kong in July 2011 and were supplied to public and private hospitals, private doctors and pharmacies. DH had alerted professional healthcare bodies about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports. A press statement was released on the same day to alert the public of the recall.

Selling any drug not of the nature, substance or quality demanded by the purchaser is an offence under Section 52(1) of the Public Health and Municipal Services Ordinance (Cap 132). The maximum penalty involved is $10,000 and three months' imprisonment.

Drug Incident

Warning on oral products containing banned and undeclared Western drug ingredients

In July 2012, DH appealed to members of the public not to buy or consume two oral products called "Conting Qianweisu Slimming Herbs Capsule"「康婷纖維素」and "Tinea Schwartz's"「癬泰舒膠囊」as they were found to contain banned and undeclared Western drugs that are dangerous to health.

DH was notified by the Hospital Authority (HA) about two patients feeling unwell after consumption of the products. Investigation showed that "Conting Qianweisu Slimming Herbs Capsule" was purchased outside Hong Kong, whereas "Tinea Schwartz's" was purchased from an Internet website. The details of these two cases are listed as follows.

Patients	Products consumed	Symptoms developed	Drug ingredients detected in laboratory test
28-year-old woman	Conting Qianweisu Slimming Herbs Capsule 「康婷纖維素」	chest pain and sweating	Sibutramine
67-year-old man	Tinea Schwartz's 「癬泰舒膠囊」	shortness of breath, fever, impaired kidney function, pneumonia and septic shock	Prednisone

Sibutramine is a Part I poison and was once a western medicine used as an appetite suppressant. Since November 2010, products containing sibutramine had been banned in Hong Kong because of the increased cardiovascular risk. Weight control should be achieved through a good diet and appropriate exercise. People ought to consult healthcare professionals before using any medication for weight control.

Prednisone is a Part I Poison and is a steroid that has strong anti-inflammatory action. Taking prednisone for a long time, especially when in substantial dosage, can cause side effects such as moon face, high blood pressure, high blood sugar and peptic ulcer. Improper use of any steroids may pose serious health risks. Patients with medical illness which require medical intervention ought to consult healthcare professionals for appropriate advice on medication. They are strongly urged not to self-medicate or use over-the-counter medication without professional supervision.

Press statements related to the cases were issued on 13 July and 19 July 2012 respectively.

Man arrested for illegal sale of unregistered pharmaceutical products

On 26 July 2012, a joint operation was conducted by DH and the Police resulting in the arrest of a 67-year-old man for suspected illegal sale of two unregistered pharmaceutical products that claim to contain glucosamine and vitamin D respectively.

Upon investigation of a complaint, Blackmores Glucosamine and Caltrate Plus with unregistered strengths and pack sizes were found to be offered for sale in an Internet auction website. In Hong Kong, Blackmores Glucosamine 500mg (HK-56134) with a pack size of 90 tablets and Caltrate Plus (HK-51984) containing 200IU of Vitamin D with a pack size of 60 tablets are registered. However, the two products sold were found to be labeled with different strengths of active ingredients, of different pack sizes and bore no Hong Kong registration number.

A press statement related to the case was issued on the same day.

Selling unregistered pharmaceutical products is an offence under the Pharmacy and Poisons Ordinance (Cap 138). The maximum penalty is a fine of $100,000 and two years' imprisonment.

Products containing sibutramine are banned and are not accepted for registration as pharmaceutical products in Hong Kong. A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. 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, disposed or submitted to the Department's Drug Office during office hours.

Useful Contact

Drug Complaint:

Tel: 2572 2068

Fax: 2147 0457 & 2123 1996

E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920

Fax: 2147 0457

E-mail: adr@dh.gov.hk

Link: http://www.drugoffice.gov.hk/adr.html

Post: ***Pharmacovigilance Unit,***
Drug Office, Department of Health,
3/F, Public Health Laboratory Centre,
382 Nam Cheong Street, 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.