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

Macau: Batch recall of Sibelium Capsule 5mg

On 7 June 2012, the Health Bureau of Macau (HBM) announced the recall of 2 lots of Sibelium Capsules 5mg (lot numbers: 9LL1800 and AEL0Y00) manufactured by Janssen-Cilag SPA of Italy because the product's stability studies showed out-of-specification results. The quantity of the active ingredient was found to be below the specification in samples tested. In order to protect the health of the public, HBM instructed importers and retail pharmacies to recall the lots concerned.

In Hong Kong, Sibelium Capsules 5mg (HK-16267) was registered by Johnson & Johnson (Hong Kong) Ltd. (Johnson) and it was used for treatment of vertigo. Johnson applied for the de-registration of the product on 1 June 2012, and then on 7 June 2012, Johnson further informed DH that the deregistration was due to the unsatisfactory stability test result and the company would replace Sibelium Capsules 5mg with Sibelium Tablets 5mg (HK-60517). Johnson further confirmed that one affected lot (lot number: 9LL1800) had been imported into Hong Kong. All stocks of Sibelium Capsules 5mg were replaced and the product was no longer registered since 15 June 2012.

China: Label update for oral products containing lamotrigine hydrochloride and misoprostol

On 8 June 2012, the State Food and Drug Administration (SFDA) of China announced the revision of the labels of oral products containing lamotrigine hydrochloride and misoprostol. For lamotrigine hydrochloride, information including the risk of severe skin rash (including Stevens Johnson Syndrome) was added on the warnings, adverse reactions and precautions sections of the product labels. For misoprostol, the boxed warning on the labels was revised to include the potential risk of miscarriage, premature birth or birth defects on pregnant woman and special precautions on its use in women of childbearing ages. Pharmaceutical manufacturers were instructed to include the updated warnings in the products' package inserts.

In Hong Kong, there are 18 and 5 oral registered pharmaceutical products containing lamotrigine and misoprostol respectively, and all are prescription medicines. Lamotrigine is an anti-epileptic drug whereas misoprostol is used in the treatment of gastric and duodenal ulcers. In view of the SFDA's recommendations, 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.

UK: Updated information for alerts of Nutriflex products

Following the global recall of Nutriflex products as reported in Issue No. 26 of Drug News, the Medicines and Healthcare Products Regulatory Agency (MHRA) of the UK issued an update on 19 June 2012 about the Nutriflex Lipid and Nutriflex Omega products. Upon the detection of potential particulate formation of Nutriflex products during stability testing, the manufacturer, B. Braun Medical Ltd., had recommended to conduct additional filtration during administration of Nutriflex Lipid products, recalled and temporarily ceased the supply of Nutriflex Omega products. B. Braun Medical Ltd. informed MHRA in June 2012 that the problem with particulates in the products had been resolved and the coming stock of Nutriflex

Lipid products which were manufactured on or after 21 March 2012 and expired after February 2014 would no longer require the additional filtration step. In addition, the marketing of Nutriflex Omega products would also resume soon.

In Hong Kong, Nutriflex Lipid Peri Emulsion for Infusion (HK-50080), Nutriflex Lipid Plus Emulsion for Infusion (HK-50081), Nutriflex Lipid Special Emulsion for Infusion (HK-50103), Nutriflex Omega Special Emulsion for Infusion (HK-60999) and Nutriflex Omega Plus Emulsion for Infusion (HK-61000) are registered by B. Braun Medical (HK) Ltd. (B. Braun). They are indicated for parenteral nutrition therapy. On 21 December 2011, DH was informed by B. Braun about a global recall of Nutriflex Lipid products and a total recall of the three products was subsequently initiated in Hong Kong on the same day. Letter to inform healthcare professionals and press release were issued on the same day. As for the Nutriflex Omega products, B. Braun confirmed that they had not been marketed in Hong Kong.

UK: Batch recall of Retin-A Gel 0.025% 60g tubes (Tretinoin)

On 20 June 2012, MHRA announced that Janssen-Cilag Ltd. recalled three batches of Retin-A Gel 0.025% 60g (lot numbers: 1E501B, 1M376A and 2A016D) from wholesalers because of the detection of a slight increase in potency during routine stability monitoring.

In Hong Kong, Retin-A Gel 0.025% (HK-13342) is registered by Johnson & Johnson (Hong Kong) Ltd. and is a prescription medicine indicated for the treatment of acne. The company confirmed that the above product had not been imported into Hong Kong since 2005 and none of the concerned batches had been imported.

Macau: Batch recall of Mega Gluco Plus Tablets

On 21 June 2012, the HBM informed DH that two batches of Mega Gluco Plus Tablets (lot numbers 105052 and 109113 with expiry dates July 2014 and November 2014 respectively) were recalled in Macau from shelf because of out-of-specification disintegration test result.

In Hong Kong, Mega Gluco Plus Tablets (HK-56820) is registered by Julius Chen & Co (HK) Ltd. and is used as a dietary supplement. Samples of Mega Gluco Plus Tablets were taken for analysis by the Government Laboratory and were found to be satisfactory in respect of the manufacturer's specification in the disintegration test. DH will keep vigilant against any updated safety and quality issue of the drug.

US: Batch recall of M-M-R® II (Measles, Mumps, and Rubella Virus Vaccine Live)

On 21 June 2012, the Food and Drug Administration (FDA) of US announced that Merck recalled one batch of M-M-R® II (lot number: 0851AA) because it had been shipped to US unintentionally. The doses from this batch were distributed in the market between 17 – 25 May 2012, and were released prior to its final internal approval. A comprehensive investigation was subsequently done which revealed no product safety, quality, or efficacy concerns. As such, it was recommended that revaccination was not necessary if product from this batch had been administered.

In Hong Kong, MMR Virus Vaccine Live (HK-01891) is registered by Merck Sharp & Dohme (Asia) Ltd. (Merck) and is a prescription medicine indicated for immunization against measles, mumps and rubella in children at or below 12 months, non-pregnant adolescents, adult females and postpartum women. As confirmed by Merck, the affected batch had not been imported into Hong Kong.

EU: Updated dosing recommendations of Doribax for treating patients with nosocomial pneumonia

As reported in Issue No. 27 of Drug News, Janssen Pharmaceuticals, Inc. terminated a clinical trial with Doribax (doripenem) in ventilator-associated pnuemonia (VAP) prematurely due to concerns about the observed higher mortality rate and lower clinical cure rate among subjects with VAP receiving a 7-day treatment of doripenem (1g every 8 hours) as compared with those with a 10-day treatment of imipenem-cilastatin (1g every 8 hours). On 22 June 2012, the European Medicines Agency (EMA) released new recommendations of Doribax for the treatment of patients with nosocomial pneumonia, including VAP. After reviewing the trial concerned and the currently available data, the Agency's Committee for Medicinal Products for Human Use (CHMP) opined that the short and fixed

duration of treatment with Doribax was a major contributing factor to the trial outcome. CHMP also considered that the effectiveness of Doribax might be affected by other factors such as augmented renal clearance and infections involving specific types of bacteria. As a result, CHMP concluded that the benefits of doribax continued to outweigh its risk but the prescribing information should be updated to allow treating certain patients of nosocomial pneumonia at a higher dose and to clarify the recommendations and warnings on its use in treating different types of bacterial infection. Healthcare professionals were advised to provide a longer treatment duration (10-14 days) for patients with nosocomial pneumonia and double the usual recommended dose to 1g every 8 hours for treating those who had augmented renal clearance and/or with infections with non-fermenting gram-negative pathogens. In addition, they were also advised to consider including aminoglycoside when treating patients of nosomial pneumonia caused by non-fermenting gram-negative pathogens.

In Hong Kong, Doribax for Inj 500mg (HK-57638) is a pharmaceutical product registered by Johnson & Johnson (Hong Kong) Ltd. and is a prescription medicine. VAP is one of the approved indications with the recommended dose of 500 mg every eight hours intravenously, given over 1 or 4 hours. Upon the release of safety news related to the early termination of the clinical trial with doribax, a letter to healthcare professionals was issued on 6 January 2012. In view of the latest EMA's recommendation, another letter was issued to healthcare professionals on 25 June 2012 and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board.

EU: Benefit-risk profile for oral tolperisone considered positive only for adults with post-stroke spasticity

On 22 June 2012, EMA issued a new recommendation to restrict the use of tolperisone for treating adults with post-stroke spasticity in oral formulation only after its review. The review was initiated in Germany because of concerns over several post marketing reports of hypersensitivity reactions and insufficently demonstrated efficacy in some indications. The efficacy of tolperisone was found to be limited in several indications and the risk of hypersensitivity reactions was more significant than identified in pre-marketing phase. As such, CHMP concluded that the benefits of tolperisone outweighed its risks only when treating adults with post-stroke spasticity and in oral formulation. CHMP also recommended to revoke the marketing authorisations of injectible tolperisone and update the product information of oral tolperisone to include the associated risk of hypersensitity reaction. Doctors were advised to stop prescribing tolperisone for any indication except post-stroke spasticity in adults and stop using injectable tolperisone. Adult patients currently using tolperisone for indications other than post-stroke spasticity or using injectable tolperisone were advised to consult their doctor for changing to an appropriate alternative treatment, and be vigilant against the symptoms of hypersensitivity reactions during treatment.

In Hong Kong, there are four registered pharmaceutical products containing tolperisone, all are in oral dosage form and are prescription medicines indicated for muscle spasms. In view of the EMA's recommendations, a letter to healthcare professionals was issued on 25 June 2012, and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board.

EU: Recommendation to restrict the use of trimetazidine-containing medicines for patients with angina pectoris

On 22 June 2012, EMA issued a new recommendation to restrict the use of trimetazidine-containing medicines in the treatment of patients with angina pectoris to second-line, add-on therapy. EMA's CHMP recommended to delete all other indications (treatment of vertigo, tinnitus and visual disturbance) from the marketing authorisation as their benefits were not sufficiently demonstrated and did not outweigh the risks. The recommendation was made after the review of trimetazidine on its efficacy and its associated risk of movement disorders. Although patients usually made a full recovery from the movement disorders within four months after discontinuation of treatment, CHMP recommended new contraindications and warnings to reduce and manage this risk. Doctors were advised not to prescribe the medicine to patients with Parkinson disease, parkinsonian symptoms, tremors, restless leg syndrome, other related movement disorders, or severe renal impairment. In addition, they were

advised to consider dose reduction in patients with moderate renal impairment and elderly patients, and discontinue trimetazidine permanently in patients who developed movement disorders.

In Hong Kong, there are seven registered pharmaceutical products containing trimetazidine and are prescription medicines. Apart from angina pectoris, they are also indicated for Meniere's disease, vertigo and/or tinnitus. In view of the EMA's recommendation, a letter to healthcare professionals was issued on 25 June 2012, and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board.

US: Label update for Cefepime on the risk of seizure in renal impaired patients without proper dosage adjustments

On 26 June 2012, the Food and Drug Administration (FDA) reminded healthcare professionals about the need to adjust the dosage of cefepime in patients with renal impairment. Cases of nonconvulsive status epilepticus associated with the use of cefepime were identifed in various medical literatures and FDA's Adverse Event Reporting System database. Most victims were patients with renal impairment who did not receive appropriate dosage adjustments of cefepime. In the majority of cases, the seizures were reversible and resolved after discontinuing cefepime and/or after hemodialysis. Healthcare professionals were reminded to adjust the dosage of cefepime in patients with creatinine clearance less than or equal to 60 mL/min in order to minimize the risk of seizures. In US, the Warnings and Precautions and Adverse Reactions sections of the cefepime label were being revised accordingly to highlight this risk.

In Hong Kong, there are four registered pharmaceutical products containing cefepime and are prescription medicines. Cefepime is a broad-spectrum cephalosporin antibiotic. In view of FDA's recommendation, a letter to healthcare professionals was issued on 27 June 2012, and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board.

Canada: Glass vial defects for 3 lots of Paclitaxel for Injection, 300mg/50ml

On 26 June 2012, Hospira Healthcare Corporation (Hospira) in consultation with Health Canada informed healthcare professionals that complaints from customers outside Canada were received regarding visible vial defects among multiple products. The vial defects might present as particles embedded in the glass vial, rust-like marks on the vial or particles in the solution. However, no defects or complaints had been reported for the three lots (Y076847AB, Y026843AB and Y046843AB) of Paclitaxel which were manufactured from the same affected empty glass vial and distributed in Canada. Healthcare professionals were reminded to visually inspect the vial for particles and not to use if any were present. They were advised to use an in-line filter with a microporous membrane not greater than 0.22 microns during the administration of Paclitaxel in accordance with the Canadian Product Monograph.

In Hong Kong, there are 2 paclitaxel-containing products, Anzatax Inj 150mg/25ml (HK-40639) and Anzatax Inj 30mg/5ml (HK-40640), and are registered by Hospira Ltd. They are prescription medicines indicated for the treatment of metastatic ovarian and breast cancer, and non-small cell lung cancer. According to the company, the three affected batches of Paclitaxel for Injection, 300mg/50ml had never been imported to HK. 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.

US: New information with ondansetron (Zofran) regarding the associated risk of QT prolongation

As reported in Issue No. 24 and No. 28 of Drug News, FDA issued alerts and relevant label changes about the associated risk of abnormal heart rhythms with ondansetron. On 29 June 2012, FDA released the preliminary results of a recently completed clinical study which suggested that a single intravenous dose of 32 mg ondansetron might affect the electrical activity of the heart (QT interval prolongation) and subsequently pre-dispose patients to develop Torsades de Pointes, an abnormal and potentially fatal heart rhythm disorder. The manufacturer of Zofran, GlaxoSmithKline, decided to further update the drug label to remove the 32 mg single intravenous dose and state that the

Safety Update

recommended dose of ondansetron for chemotherapy-induced nausea and vomiting was 0.15 mg/kg administered every 4 hours for three doses and no single intravenous dose should exceed 16 mg. The new information on QT prolongation did not change any recommended oral dosing regimens for ondansetron.

In Hong Kong, there are 24 registered pharmaceutical products containing ondansetron and seven of them were injectable products. They are prescription medicines used for the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy, and prevention and treatment of postoperative nausea and vomiting. In response to a relevant alert issued by FDA earlier in September 2011, a letter was sent to inform healthcare professionals on 16 September 2011 and the Registration Committee of the Pharmacy and Poisons Board discussed the issue on 28 February 2012 which decided to include safety information on the associated risk of QT prolongation and Torsades de Pointes on the drug label. In view of FDA's latest recommendation, a letter to inform healthcare professionals was issued on 3 July 2012, and the matter will be further discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board.

Drug Recall

Total recall of Derma Skin Spray (HK-54689)

On 4 June 2012, DH endorsed a licensed drug manufacturer, Meyer Pharmaceuticals Ltd. (Meyer), to recall from market all batches of "Derma Skin Spray"「百癬靈特效皮膚噴霧」as some sale packs of the product bore unapproved labels which rendered the product unregistered. Derma Skin Spray contains salicylic acid and is an over-the-counter medicine used for the treatment of athlete's foot.

The matter came to light upon DH's investigation into a public enquiry relating to the product. Investigation revealed that Meyer had sold the product to a distributor, Forward Medicine Ltd. (Forward) whom in turn sold the product to local retailers. Forward was found to relabel some sale packs of the product without authorization during the course of distributing the product.

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 of the product concerned and a press statement was released on the same day to alert the public of the recall.

The illegal manufacture of pharmaceutical products and sale of unregistered pharmaceutical products are both 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.

Total recall of Bandi Enema (HK-48262)

On 27 June 2012, DH instructed a licensed drug wholesaler, Hengan Pharmacare Co Ltd. (Hengan), to recall from market all batches of "Bandi Enema"「便利通浣腸」because of quality concerns. Bandi Enema, manufactured in Taiwan by Tien Chien Pharmaceutical Co Ltd, is an over-the-counter medicine containing glycerin and sodium chloride for the relief of constipation.

Through DH surveillance programme, DH was informed by the Government Laboratory that a sample of Bandi Enema was found to contain higher than registered levels of glycerin (0.14g/ml instead of 0.1g/ml) and sodium chloride (0.14g/ml instead of 0.05g/ml). Although there was no safety issue, the quality concern of the product warranted a total recall.

Bandi Enema was imported into Hong Kong then supplied to retail outlets and exported to Macau. DH had alerted professional healthcare bodies and the Macau authority about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports of the product concerned and 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 is a fine of $10,000 and three months' imprisonment.

Drug Incident

Warning on oral products containing banned and undeclared Western drug ingredients

In June 2012, DH appealed to members of the public not to buy or consume two oral products called "Jin Tan 1-Ching-Sung Laxative Tablets"「金壇一輕鬆通便片」and "Dong Qing San Bian Li"「動情三鞭粒」as they were found to contain banned and undeclared Western drugs that were dangerous to health.

DH was notified by the Hospital Authority (HA) about two patients feeling unwell after consumption of the products concerned. They obtained their products outside Hong Kong and the details of these two cases were listed as follows:

Patients	Products consumed	Symptoms developed	Drug ingredients detected in laboratory test
71-year old woman	Jin Tan 1-Ching-Sung Laxative Tablets 「金壇一輕鬆通便片」	epigastric discomfort, right upper quadrant abdominal pain and passing tea-coloured urine	Diacetyldiphenolisatin (also known as oxyphenisatin)
81-year old man	Dong Qing San Bian Li 「動情三鞭粒」	palpitation, shortness of breath, chest discomfort and irregular heart rate	Sildenafil

Diacetyldiphenolisatin was banned for its hepatotoxicity in Hong Kong in 1997. It was used previously for treating constipation.

Sildenafil is a Part I Poison used for treating male sexual dysfunction. Its side effects include low blood pressure, headache, vomiting, dizziness, and transient vision disturbances. It may interact with some drugs (such as nitroglycerin for treatment of angina) and cause decrease in blood pressure to dangerous levels. Improper use of sildenafil may pose serious health risks, especially for patients with heart problems.

Press statements related to the cases were issued on 1 June and 13 June 2012 respectively.

Patients with any chronic disease are advised to consult healthcare professionals for appropriate advice and management. They are strongly urged to refrain from self-medication or using over-the-counter products without professional supervision.

Persons arrested for selling unregistered pharmaceutical products

On 12 June and 25 June 2012, joint operations were conducted by DH and the Police resulting in the arrests of a 29-year-old woman for suspected illegal sale of one box of a slimming product, "Shan Dian Shou"「閃電瘦」, and a 40-year-old man for suspected illegal sale of two unregistered pharmaceutical products containing glucosamine, namely Webber Naturals Glucosamine Chondroitin MSM and Webber Naturals Glucosamine Chondroitin Extra Strength respectively. DH issued press statements on the days of respective operations.

For the former case, the slimming product had been obtained earlier from an Internet auction website during DH's surveillance operation and was found to contain sibutramine, phenolphthalein and sildenafil.

Sibutramine is a Part I poison and was once a western medicine used as an appetite suppressant. Since November 2010, products containing sibutramine have been banned because of increased cardiovascular risk. Phenolphthalein was once used for treating constipation but was banned for its cancer-causing effect.

Weight control should only be achieved through a good diet and appropriate exercise. People ought to consult healthcare providers for professional advice if they have questions and definitely before using any medication for weight control.

For the latter case, the two unregistered pharmaceutical products concerned were found to be sold in an Internet auction website during the investigation of a complaint. The man was found in possession of 17 bottles of unregistered pharmaceutical products containing glucosamine during the joint operation. Glucosamine is used in musculoskeletal and joint disorders.

Products containing sibutramine or phenolphthalein 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. Part I poisons such as sildenafil must not be sold on Internet. They must be sold at registered pharmacy by a registered pharmacist or under his or her supervision. In addition, products containing sildenafil can only be sold with a doctor's prescription. Sale or possession of unregistered pharmaceutical product, and illegal sale or possession of Part I poison are offences under the Ordinance and the maximum penalties for each offence is $100,000 fine and two years' imprisonment.

As unregistered pharmaceutical products have not been evaluated by the Board, their product safety, quality and efficacy may not be guaranteed. Members of the public are urged not to buy or use products of unknown or doubtful composition from the market or the Internet. They should consult healthcare professionals for advice if they feel unwell after taking the product concerned. Members of the public who have bought the above products should stop using them immediately and should submit them to the department's Drug Office at 3/F., Public Health Laboratory Centre, 382 Nam Cheong Street, Kowloon, during office hours for disposal.

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.