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

UK, Singapore, US: Batch recall of an Anti-thymocyte Globulin (Rabbit) 25mg/vial

The Medicines and Healthcare Products Regulatory Agency (MHRA) of UK, the Health Sciences Authority (HSA) of Singapore and the Food and Drug Administration (FDA) of US announced on 6 August, 14 August and 28 August 2012 respectively that an Anti-thymocyte Globulin (Rabbit) 25mg/vial were recalled by Genzyme. Four batches (lot numbers: C0066H06, C0074H08, C0088H08 and C0102H11), two batches (lot numbers: C0074 and C0088) and nine batches (lot numbers: C0062C01, C0072C01, C0086C01, C0094C01, C0096C01, C0098C01, C0098C02, C0098C03 and C0100C01) were recalled in UK, Singapore and US respectively. The recall was initiated when one Thymoglobulin lot (C0072) failed a periodic stability test for the molecular size distribution test. Additional lots, manufactured with comparable quality of the raw material, were being recalled based on the potential risk for a stability failure prior to end of shelf life for aggregation. No other Thymoglobulin lots were involved in this recall.

In Hong Kong, Thymoglobuline for IV Injection 25mg/5ml (HK-33039) is registered by Sanofi-Aventis HK Ltd. (Sanofi-Aventis). It contains anti-thymocyte immunoglobulins and is manufactured by Genzyme Polyclonals S.A.S. in France. It is a prescription medicine indicated for the treatment of graft rejection in transplantation and aplastic anaemia. On 3 August 2012, the Department of Health (DH) endorsed the recall of three affected batches (lot numbers: C0074H29, C0088H10 and C0102H03) by Sanofi-Aventis. Press release regarding the recall was issued on the same day. The details of the recall was reported in the section of "Drug Recall" of this Drug News.

US: Codeine use in certain children after tonsillectomy and/or adenoidectomy may lead to rare, but life-threatening adverse events or death

On 15 August 2012, FDA reminded healthcare professionals about the risks of using codeine in children, particularly in those who have undergone tonsillectomy and/or adenoidectomy for obstructive sleep apnoea syndrome (OSAS), and that the lowest effective dose of codeine for the shortest period of time should be used on an as-needed basis. It was noted that recent literature has reported three pediatric deaths and one non-fatal but life threatening case of respiratory depression in children who have taken codeine for pain relief after tonsillectomy and/or adenoidectomy for OSAS. These children who were two to five years old, had evidence of an inherited ability to convert codeine into life-threatening or fatal amounts of morphine in the body, though all had received doses of codeine that were within the typical dose range. In addition, parents and caregivers were also reminded to observe any signs of morphine toxicity, such as unusual sleepiness, confusion, or difficult or noisy breathing in their child and should seek medical attention immediately.

In Hong Kong, there are about 362 registered codeine-containing pharmaceutical products and most of them are in syrup form. They are indicated to relieve pain and cough. So far, Drug Office had not received any relevant adverse event report. In view of FDA's recommendation, a letter to healthcare professionals was issued on 16 August 2012. DH will keep vigilant against any updated safety issue of the products.

UK: Echinacea products should not be used in children under 12 years old

On 20 August 2012, MHRA alerted the public not to use oral Echinacea products for children under 12, which was the precautionary advice from the European Herbal Medicinal Products Committee and the UK Herbal Medicines Advisory Committee. Both Committees concluded that the perceived benefits of the use of Echinacea in children under 12 were outweighed by the potential risks in this age-group and there was a low risk of allergic reactions but these could be severe. Children aged 12 or over and adults could continue to use oral Echinacea products. Risks of side effects in older children and adults were reduced because they weighed more and in general caught fewer colds. MHRA was working with the herbal sector to ensure that all oral Echinacea products were re-labelled with this new warning.

In Hong Kong, there are five registered Echinacea-containing pharmaceutical products which are indicated as nutritional supplements. In view of the latest recommendation from MHRA, the issue will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

UK: Batch recall of Zovirax Suspension 200mg/5ml

On 22 August 2012, MHRA announced that GlaxoSmithKline (GSK) UK recalled 13 batches of Zovirax Suspension 200mg/5ml (Aciclovir) 125ml bottles from wholesalers, pharmacies and clinics. This was due to incorrect dosing instructions in the patient information leaflet advising patients to take half the recommended dose.

In Hong Kong, Zovirax Suspension Oral 200mg/5ml (HK-25758) is registered by GSK Ltd. It is a prescription medicine indicated for viral infections. GSK confirmed that the affected batches had not been imported to Hong Kong.

Singapore: Latest updates on the risk of lymphoma with topical calcineurin inhibitors

On 24 August 2012, HSA announced the new safety updates on the risk of malignancy related to topical calcineurin inhibitors (TCIs), namely tacrolimus (Protopic® ointment) and pimecrolimus (Elidel® cream). In May 2011, the findings of epidemiology studies (including increased risk of lymphoma, particularly T-cell lymphoma, in TCI-treated atopic dermatitis patients) were discussed in a Paediatric Advisory Committee (PAC) meeting held by FDA. The PAC agreed that the findings specifically to the paediatric population and to the long-term safety profile of TCIs remained questionable, and concurred that the current US product insert labelling adequately represented the risks and benefits of Protopic® and Elidel®. Healthcare professionals were reminded to adhere to the following precautions to minimise the risks of TCIs which were reflected in the local package insert of Protopic® and Elidel® in Singapore:

- continuous long-term use of TCIs in any age group should be avoided, and application should be limited to the affected areas;
- TCIs were not indicated for use in children less than 2 years of age;
- use of topical tacrolimus in children aged 2 to 16 years of age was restricted to the lower strength preparation (Protopi® 0.03% ointment);
- TCIs should not be applied to lesions that were considered to be potentially malignant or pre-malignant;
- lymphadenopathy present at initiation of therapy should be investigated and kept under review. Patients who received TCIs, and who developed lymphadenopathy should be monitored to ensure that the lymphadenopathy resolved. In case of persistent lymphadenopathy, the aetiology of the lymphadenopathy needed to be investigated. In the absence of a clear aetiology for the lymphadenopathy or in the presence of acute infectious mononucleosis, discontinuation of therapy should be considered; and
- TCIs should not be used in patients with congenital or acquired immunodeficiencies or in patients on therapy that caused immunosuppression. Excessive exposure of the skin to ultraviolet light including light from a solarium, or therapy with PUVA (psoralen and ultraviolet A [UVA]), UVA or ultraviolet B (UVB) should be avoided during treatment with TCIs.

Safety Update

In Hong Kong, Protopic Oint 0.1% (HK-48906) and Protopic Oint 0.03% (HK-48907) are registered by Astellas Pharma HK Co. Ltd., and Elidel Cream 1% (HK-51217) is registered by Novartis Pharmaceuticals (HK) Ltd. They are prescription medicines indicated for patients aged 2 years and over with mild or moderate atopic dermatitis. The safety information mentioned above has been included in the labelling of the products. DH will keep vigilant against any updated safety and quality news of the issue.

US: FDA recommends against use of Revatio (sildenafil) in children with pulmonary hypertension

On 30 August 2012, FDA recommended that Revatio (sildenafil) should not be prescribed to children (ages 1 to 17) for pulmonary arterial hypertension (PAH). This recommendation was based on a recent long-term clinical paediatric trial showing that a higher risk of mortality was found in children taking a high dose of Revatio than those taking a low dose, and the low doses of Revatio were not effective in improving exercise ability. Most deaths were caused by pulmonary hypertension and heart failure, which were the most common causes of death in children with PAH. In US, Revatio was approved to improve exercise ability and delay clinical worsening of PAH in adult patients only and the maximum recommended dose is 20mg three times a day. In view of the findings, the labeling of Revatio had been revised to state the use of Revatio was not recommended in paediatric patients and to include the results of the mentioned trial. Healthcare professionals were reminded that use of this product, particularly chronic use, was not recommended in children.

In Hong Kong, Revatio Tab 20mg (HK-54170) is registered by Pfizer Corp. HK Ltd. It is a prescription medicine indicated for the treatment of PAH in adult patients (≥ 18 years) with the maximum recommended dose of 20mg three times a day. The use of sildenafil was not recommended in children and adolescents (< 18 years). A letter to healthcare professionals was issued on 31 August 2012. DH will keep vigilant against any updated safety and quality issue of the product.

Drug Recall

Batch recall of Thymoglobuline for IV Injection 25mg/5ml (HK-33039)

On 3 August 2012, DH endorsed a licensed drug wholesaler, Sanofi-Aventis HK Ltd. (Sanofi), to recall from market three batches of Thymoglobuline for IV Injection 25mg/5ml (lot numbers: C0074H29, C0088H10 and C0102H03), because of a stability issue. Thymoglobuline is indicated for the prophylaxis and treatment of graft rejection in transplantation. It 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 product's French manufacturer, Genzyme Polyclonals S.A.S., (Genzyme), found that one batch (lot number: CC0072) of the product failed to meet the specifications during an ongoing stability study. This batch was only sold in the US. As a precautionary measure, Genzyme initiated a global recall of all batches manufactured under the same condition of the failed batch. According to the finding of Genzyme, none of the other batches failed to meet the specifications.

The three affected batches were supplied to the Hospital Authority (HA) and some vials of one batch (lot number: C0074H29) were exported to Macau. DH had alerted HA, 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 in connection with the product. A press statement was released on the same day to alert the public of the recall.

Total recall of Antacaine Suspension (HK-23691)

On 8 August 2012, DH instructed a licensed manufacturer, Quality Pharmaceutical Lab. Ltd. (Quality) to recall from market all batches of Antacaine Suspension 3.6 Litres because of quality issue. Antacaine is indicated for relief of heartburn and indigestion and can only be sold under the supervision of pharmacists at registered dispensaries.

Drug Recall

During a recent Good Manufacturing Practice inspection, the pH result of a stability test of a batch of the product was found higher than specification. Further samples were tested and the pH of some of these samples was found to be higher than specification. Though the increase in pH would not affect the safety and efficacy of the product, DH instructed Quality to recall all batches of the products a precautionary measure.

The product had been supplied mainly to private doctors, two private hospitals, two veterinary clinics and some pharmacies in Hong Kong. DH had alerted the private hospitals and professional healthcare bodies about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports in connection with the product. 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 a $10,000 fine and three months' imprisonment.

Total recall of unregistered version of Vimpat Tablets 50mg (HK-61175) and 100mg (HK-61176)

On 14 August 2012, DH instructed a licensed wholesaler, Orient Europharma Co. Ltd. (Orient Europharma), to recall from market all batches of Vimpat Tablets 50mg and 100mg as the company had imported and distributed the unregistered version of the products containing soya lecithin coating. In Hong Kong, Vimpat Tablets 50mg and 100mg are registered without soya lecithin coating and are indicated for the treatment of epilepsy. They are prescription medicines which can only be sold with doctor's prescription and under the supervision of pharmacists at registered pharmacies.

Orient Europharma imported 506 boxes of Vimpat Tablets 50mg and 497 boxes of Vimpat Tablets 100mg to Hong Kong in July this year. Eleven boxes of Vimpat Tablets 50mg and nine boxes of Vimpat Tablets 100mg were sold to local pharmacies and private doctors. 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 in connection with the products. A press statement was released on the same day to alert the public of the recall.

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

Members of the public who have the products in hand should not stop medication but should seek advice from healthcare professionals. If they are in doubt or feeling unwell after taking the products they should consult their healthcare providers.

Drug Incident

Warning on slimming product with undeclared and banned drug ingredients

On 17 August 2012, DH appealed to members of the public not to buy or consume a slimming product bearing the Chinese name "Sheng Yuan Fang" 「生源坊」 printed on its green capsules, as it may contain undeclared and banned drug ingredients that are dangerous to health.

DH was notified by HA about a 27-year-old lady who was hospitalized because of loss of consciousness for a brief period, after consumption of the above slimming product. The laboratory test finding on the product sample showed the presence of an undeclared Western drug, sildenafil, and two banned Western drugs, sibutramine and phenolphthalein. The patient purchased the product from an Internet site.

DH previously identified similar products bearing the name of "Sheng Yuan Fang" adulterated with undeclared and banned western drug ingredients. Press releases were issued on 31 May 2010 and 24 February 2012 to alert the public not to consume the product.

Drug Incident

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

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

Weight control should be achieved through balanced diet and appropriate exercise. People should consult health-care professionals before using any medication for weight control.

Persons arrested for illegal sale of unregistered pharmaceutical products and illegal sale of Part I poisons

On 1 August and 8 August 2012, joint operations were conducted by DH and the Police resulting in the arrests of a 33 year-old man for suspected illegal sale of unregistered pharmaceutical product called Men's Rogaine Topical Aerosol, and a 29 year-old woman for suspected illegal sale of unregistered pharmaceutical product called Rapid and Clean Cream – SM Cream. DH issued press statements on the days of operations.

For both cases, complaints were received alleging the unregistered medicines were offered for sale on Internet. Investigation revealed that the products were not pharmaceutical products registered with the Pharmacy and Poisons Board and contained substances which are Part I poisons.

For the former case, the product contained an ingredient of pharmaceutical product, minoxidil, which is a Part I poison and should be sold at pharmacy under the supervision of registered pharmacist. Minoxidil is commonly used for hair loss treatment. The side effects include scalp irritation and itchiness.

For the latter case, the product contained an ingredient of pharmaceutical product, 9.6% lignocaine, which is a Part I poison and should be sold at pharmacy under the supervision of registered pharmacist. Cream containing lignocaine is commonly used as a local anaesthetic to relieve pain caused by cuts and burns, abrasions and minor procedures. Common side effect includes hypersensitivity reaction.

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 minoxidil and lignocaine must not be sold on Internet. They must be sold at registered pharmacy by a registered pharmacist or under his or her supervision. Possession or sale of unregistered pharmaceutical product and possession or sale of Part I poison are offences under the Pharmacy and Poisons Ordinance (Cap 138). The maximum penalty is a $100,000 fine and two years' imprisonment for each offence.

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 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.