Drug News
藥 物 情 報

Issue Number 42

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in April 2013 with relevant information update before publish. For the latest news and information, please refer to public announcements or the website of the Drug Office of the Department of Health (http://www.drugoffice.gov.hk).

Safety Update

Singapore: Communication on cases of necrotising fasciitis reported with Avastin® (bevacizumab)

On 9 April 2013, the Health Sciences Authority (HSA) of Singapore announced that Roche (i.e. the drug company) informed healthcare professionals of cases of necrotising fasciitis reported with Avastin® (bevacizumab). In Roche's clinical trials safety database, cases of necrotising fasciitis were reported in 0.03% (4 out of 12,845 cases) of Avastin®-treated patients compared to none in the control arms. From Roche's global post-marketing safety database, 52 patients with necrotising fasciitis were identified. Majority of the patients had gastrointestinal perforation, fistula formation or wound healing complications preceding the development of necrotising fasciitis. Some of these patients died due to complications of necrotising fasciitis. It was recommended to discontinue Avastin® and to promptly initiate appropriate therapy upon the diagnosis of necrotising fasciitis. The package insert for Avastin® would be updated to reflect the new safety information.

In Hong Kong, there are six Avastin products registered by Roche HK Ltd. (Roche), namely Avastin Roche Inj 400mg/16ml (HK-53548), 100mg/4ml (HK-53549), 400mg/16ml (Switzerland) (HK-56637), 100mg/4ml (Switzerland) (HK-55638), Avastin Roche Concentrate for Solution for Infusion 400mg/16ml (Germany) (HK-59449) and 100mg/4ml (Germany) (HK-59450). They are prescription only medicines indicated for treatment of metastatic breast, colorectal, lung, renal cancer and glioblastoma. Roche issued a Dear Healthcare Professional Communication about this new safety information on 12 April 2013 and submitted the application to change the package insert by including the relevant safety information. The Department of Health (DH) had not received any related event report in connection with the use of the products, and will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

EU: Outcome of Periodic Safety Update Report assessment leads to recommendation to restrict use of Protelos/Osseor (strontium ranelate)

On 11 April 2013, the European Medicines Agency's (EMA)'s Pharmacovigilance Risk Assessment Committee (PRAC) had recommended restrictions in the use of Protelos/Osseor (strontium ranelate), following the evaluation of data showing an increased risk of heart problems, including heart attacks. During the assessment, data from clinical studies in post-menopausal women were evaluated, showing a higher risk of heart attacks with Protelos/Osseor than with placebo, with no observed increase in mortality risk. Given the other serious risks (blood clots and rare serious skin reactions) previously identified with the medicine, PRAC concluded that a further in-depth evaluation of the benefits and risks of the medicine was needed. The outcome of PRAC's assessment was sent to EMA's Committee for Medicinal Products for Human Use (CHMP) for a final opinion. After the meeting on 25 April 2013, CHMP announced the following recommendations on the use of Protelos/Osseor:

- Protelos/Osseor should only be used for the treatment of severe osteoporosis in postmenopausal women at high risk of fracture and severe osteoporosis in men at increased risk of fracture;

- Protelos/Osseor was contraindicated in patients with a current or past history of ischaemic heart disease, peripheral arterial disease, or cerebrovascular disease, or in patients with uncontrolled hypertension;
- treatment with Protelos/Osseor should only be started by a physician experienced in the treatment of osteoporosis;
- physicians should base their decisions to prescribe Protelos/Osseor on an assessment of the individual patient's risks. The patient's risk of developing cardiovascular disease should be evaluated before and at regular intervals during treatment; and
- treatment should be stopped if the patient developed ischaemic heart disease, peripheral arterial disease or cerebrovascular disease or if hypertension became uncontrolled.

In Hong Kong, Protos Granules for Oral Suspension 2g (HK-53835) containing strontium ranelate is registered by Servier HK Ltd., and is a prescription only medicine used for the treatment of osteoporosis in postmenopausal women to reduce the risk of fracture at spine and hips. Safety alerts on the risks of venous thromboembolism and severe skin reactions were reported in Drug News Issues No. 23, No. 25, No. 29 and No. 41. A letter to healthcare professionals was issued on 19 March 2012 regarding the contraindicated use in immobilised patients or patients with venous thromboembolism. The issues had been 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 in February 2013. The Committee decided that the sales pack or package insert should be updated to include the appropriate safety information as stated in Drug News Issue No. 41. In veiw of the new safety information on cardiovascular events from EMA, another letter was issued on 15 April 2013, and the matter will be further discussed in the meeting of the Registration Committee.

Canada: Possible risk of developing atherosclerosis-related conditions with the use of Tasigna™ (nilotinib)

On 12 April 2013, Novartis Pharmaceuticals Canada Inc., in collaboration with Health Canada, announced about the reports of atherosclerosis-related diseases in patients during clinical trials and post marketing experience with the use of Tasigna™ (nilotinib). In a Phase III study in newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia patients, atherosclerosis-related diseases such as peripheral arterial occlusive disease, femoral artery stenosis, coronary artery stenosis, carotid artery stenosis, and cerebrovascular accident were reported in patients taking Tasigna™ (5.0% for Tasigna™ 300 mg BID and 6.1% for Tasigna™ 400 mg BID). A review of the Novartis global safety database search (between 1 January 2005 and 31 January 2013) identified a total of 277 cases of atherosclerosis, of which 14 were Canadian cases. The Canadian Product Monograph for Tasigna™ was revised to include these new recommendations. Healthcare professionals were recommeded to follow current clinical guidelines for the diagnosis and management of patients with signs and symptoms of events due to atherosclerosis.

In Hong Kong, Tasigna Cap 200mg (HK-56797) and Tasigna Cap 150mg (HK-60833) are prescription only medicines registered by Novartis Pharmaceuticals (HK) Ltd. (Novartis), and are indicated for the treatment of Philadelphia chromosome positive chronic myeloid leukemia. In view of Health Canada's announcement, a letter to healthcare professionals was issued on 16 April 2013. Regarding this issue, Novartis had submitted the application to change the package insert by including the relevant safety information. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

Singapore: Risk of atypical femoral fracture with the use of Xgeva® (denosumab 120 mg)

It was noted from HSA website on 18 April 2013 that GlaxoSmithKline in Singapore notified healthcare professionals of the risk of atypical femoral fractures with Xgeva® (denosumab 120 mg) use. GlaxoSmithKline had evaluated the potential for atypical femoral fractures in patients treated with Xgeva® in clinical trials and the postmarketing setting. A single case of atypical femoral fracture was reported in the open label extension phase of an ongoing clinical trial of Xgeva® in men with hormone-refractory prostate cancer. To communicate this important information, the Xgeva® package insert was

updated with a new warning on atypical femoral fracture and the inclusion of atypical femoral fracture as an adverse drug reaction.

In Hong Kong, Xgeva Solution for Injection 120mg (HK-61163) is registered by GlaxoSmithKline Ltd. (GSK) and is a prescription only medicine. Xgeva is indicated for the prevention of skeletal related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours. Regarding this issue, GSK had submitted the application to change the package insert by including the relevant safety information. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

Singapore: Important change to frequency of serum liver test monitoring for hepatotoxicity with Votrient® (pazopanib)

On 25 April 2013, GlaxoSmithKline in Singapore informed healthcare professionals of an important safety update regarding a change in frequency of serum liver test monitoring for hepatotoxicity during use of Votrient® (pazopanib). Votrient® is a kinase inhibitor indicated for the treatment of patients with advanced renal cell carcinoma and for patients who have received prior cytokine therapy for advanced disease. Healthcare professionals were advised to monitor serum liver tests before initiating Votrient® and at Weeks 3, 5, 7, and 9. Thereafter, patients should be monitored at Months 3 and 4, and as clinically indicated. Periodic monitoring should continue after Month 4.

In Hong Kong, Votrient Tab 200mg (HK-60351) and Tab 400mg (HK-60352) are prescription only medicines registered by GSK Ltd., and are indicated for the treatment of advanced renal cell carcinoma and for patients who have received prior cytokine therapy for advanced disease. GSK issued a Dear Healthcare Professional Communication about this safety information on 2 April 2013. Regarding this issue, GSK had submitted the application to change the package insert by including relevant safety information. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

US: Potiga (ezogabine) linked to blue skin discoloration and retinal abnormalities

On 26 April 2013, the Food and Drug Administration (FDA) of the US warned the public that the anti-seizure medication Potiga (ezogabine) could cause blue skin discoloration and eye abnormalities characterized by pigment changes in the retina. The skin discoloration in the reported cases appeared as blue pigmentation, predominantly on or around the lips or in the nail beds of the fingers or toes, but more widespread involvement of the face and legs had also been reported. Scleral and conjunctival discoloration, on the white of the eye and inside eyelids, had been observed as well. In some cases, retinal abnormalities had been observed in the absence of skin discoloration. FDA recommended that all patients taking Potiga should have a baseline eye exam and periodic eye exams that should include visual acuity testing and dilated fundus photography. Patients who were taking Potiga and develop any changes in the vision or any discoloration of the skin should contact the healthcare professionals right away. Patients should not stop taking Potiga without talking to the healthcare professionals, as stopping such treatment suddenly could cause serious and life-threatening medical problems. FDA was working with the manufacturer to gather and evaluate all available information to better understand these events, and would update the public when more information is available.

In Hong Kong, there are five registered pharmaceutical products containing retigabine (International Nonproprietary Name), which is the synonym of ezogabine (United States Adopted Name). The five products are Trobalt Film-coated Tab 200mg (HK-61378), 400mg (HK-61379), 50mg (HK-61380), 100mg (HK-61381) and 300mg (HK-61382), and all are prescription only medicines registered by GSK Ltd. They are indicated as an adjunctive treatment of partial onset seizures with or without secondary generalisation in adults aged 18 years and above with epilepsy. GSK issued a Dear Healthcare Professional Communication about this new safety information on 30 April 2013. Regarding this issue, GSK had submitted the application to change the package insert by including relevant safety information. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

Drug Recall

Recalls of pharmaceutical products manufactured by Celogen Pharma Pvt Ltd

On 5 April 2013, DH instructed a licensed drug wholesaler, Batou Ltd. (Batou), to recall from consumers all batches of Celonol 50 Tablets (HK-57702) as the drug failed to meet the relevant pharmacopoeial standards. Upon the investigation of a public enquiry, samples of Celonol 50 Tablets were collected by DH and anaylsis showed that the samples had exceeded the pharmacopoeial limit for total bacterial count.

During the investigation on 5 April 2013, samples of other registered pharmaceutical products manufactured by the same manufacturer, Celogen, available for sale in Hong Kong, were collected for examination. Test results showed that samples of three products, namely, Celonol 25 Tablets (HK-57137), Celevox 500 Tablets (HK- 58417) and Melcicam Tablets 7.5mg (HK- 57272), had also exceeded the limit for total bacterial count. Microbial contamination of a pharmaceutical product may not only potentially affect the therapeutic efficacy of the product, but also lead to the risk of infection for the user. Hence on 15 April 2013, DH instructed Batou to recall the three products concerned and, as a precautionary measure, all remaining registered pharmaceutical products available in Hong Kong manufactured by Celogen.

A total of 33 pharmaceutical products manufactured by Celogen are registered in Hong Kong. Among these products, 11 products have been imported for local sale and distribution. All these products are prescription only drugs and should only be used under medical supervision. Pharmacies can only sell the drugs under the supervision of a registered pharmacist and upon a doctor's prescription.

According to Batou, these products were supplied to private doctors and dispensaries. DH had alerted the concerned parties about the matter and closely monitored the recall. At the time of investigation, DH had not received any adverse drug reaction reports in connection with the products. DH had issued letters to healthcare professionals to alert them of the recall on 5 April and 15 April 2013. Press statements were also released on the same days to alert the public of the recall.

Members of the public who are taking the products should seek advice from their doctors immediately for an alternative supply of medicines for continued treatment.

Total recall of A-Lices Scalp Hygiene Shampoo 1% (HK-59822)

On 18 April 2013, DH endorsed a licensed drug wholesaler, Hoepharma (HK) Ltd., to recall from shelves all batches of a pharmaceutical product, namely, A-Lices Scalp Hygiene Shampoo 1%, due to a quality issue. The product is an over-the-counter pharmaceutical product used for the treatment of head lice.

DH received notification from Hoepharma that the manufacturer in Malaysia found that four batches of A-Lices Scalp Hygiene Shampoo 1% had failed an assay test during post-market evaluation. The active ingredient, malathion, was found to be lower than that was stated in the product specifications and the manufacturer was uncertain about the stability of the product. The failure in the assay test may affect the efficacy of the product. As a precautionary measure, the manufacturer decided to recall all batches of the product from the market.

According to Hoepharma, a total of 18,339 bottles of the product were imported into Hong Kong since registration in 2010. The product was supplied to public and private hospitals, DH clinics, private doctors and pharmacies. DH had alerted the concerned parties about the matter and closely monitored the recall. At the time of investigation, 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 is a $10,000 fine and three months' imprisonment.

Drug Incident

Public urged not to buy or use Steelman Capsules 2 with undeclared and controlled ingredient

On 11 April 2013, DH urged the public not to buy or use a product called "Steelman Capsules 2" as it was found to contain an undeclared and controlled ingredient.

During DH's market surveillance exercise, samples of "Steelman Capsules 2" were purchased for analysis by the Government Laboratory. Test results showed that the product contains aminotadalafil, an analogue of the virility drug ingredient tadalafil. Aminotadalafil, being chemically similar to tadalafil, is expected to pose similar health risks and it is a Part I poison under the Pharmacy and Poisons Ordinance (Cap 138). The product is not a registered pharmaceutical product in Hong Kong.

The product's distributor, Top Harvest Pharmaceuticals Co. Ltd. (Top Harvest), was raided and 439 boxes of Steelman Capsules 2 were seized. According to Top Harvest, the product was imported from the United States into Hong Kong and about 19,500 boxes had been supplied to local dispensaries and medicine companies since 2012. DH had alerted the concerned parties about the matter and closely monitored the recall. Top Harvest was instructed to recall all Steelman Capsules 2 from the market.

Tadalafil is a virility drug which should only be used under the advice of a doctor and be supplied at pharmacies under the supervision of a registered pharmacist and upon a doctor's prescription. The side effects of tadalafil 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 may cause decrease in blood pressure to dangerous levels. Improper use of tadalafil may pose serious health risks, especially for patients with heart problems.

Public urged not to buy or use slimming products with undeclared and/or banned drug ingredients

In April 2013, DH appealed to members of the public not to buy or consume unlabelled slimming products and a slimming product called "Aisiyuan (艾思源) V26 Coffee Slimming granules", as those products were found to contain undeclared and/or banned drug ingredients that are dangerous to health.

DH was notified by the Hospital Authority (HA) about the patients feeling unwell after consumption of the above-mentioned products. Investigation showed that the products were obtained from friends who had purchased the products from the Internet. The details of these two cases were summarized as follows:

Patients	Products consumed	Symptoms developed	Drug ingredients detected in laboratory test
22-year-old female patient	Four unlabelled products	Palpitation and hypokalaemia	Sibutramine, hydrochlorothiazide, fluoxetine and bisacodyl
42-year-old female patient	Aisiyuan (艾思源) V26 Coffee Slimming granules	Unconsciousness	Sibutramine

Sibutramine is a Part I poison and was once used as an appetite suppressant. Since November 2010, all products containing sibutramine have been banned because of an increased cardiovascular risk. Hydrochlorothiazide is a diuretic and is also used for the treatment of hypertension. It may cause hypotension and electrolyte imbalance. Fluoxetine is used for depression and may cause postural hypotension and alopecia. Hydrochlorothiazide and fluoxetine are both Part I poisons, and must be sold with prescriptions at pharmacies under the supervision of pharmacists. Bisacodyl is a laxative that may cause abdominal pain.

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

Press statements related to the cases were issued on 17 April and 18 April 2013 respectively.

Drug Incident

Persons arrested for illegal sale of slimming products with banned drug ingredients on the Internet

In April 2013, two joint operations were conducted by DH and the Police resulting in the arrests of various persons. Press statements related to the cases were issued on the days of the operations. The details of these cases were summarized as follows:

Case No.	Products consumed	Drug ingredients	Arrested persons
1.	Conting Qianweisu Slimming Herbs Capsule (康婷纖維素)	Sibutramine and phenolphthalein (both undeclared and banned drug substances)	A 27-year-old woman
2.	Four unlabelled products	Sibutramine, hydrochlorothiazide, fluoxetine and bisacodyl	A 34-year-old man

Phenolphthalein was used previously to treat constipation, but has been banned for its possible cancer-causing effect.

This was the third incidence of news relating to "Conting Qianweisu Slimming Herbs Capsule" and the previous cases were reported in Drug News Issues No. 33 and 41.

Retail shops raided for selling and possession of unregistered pharmaceutical products

In April 2013, three joint operations were conducted by DH and the Police resulting in the shops raided for selling and possession of unregistered pharmaceutical products. Members of public are urged not to buy or consume unregistered pharmaceutical products as they have not been evaluated by the Pharmacy and Poisons Board and their safety, quality and efficacy are not guaranteed. Press statements related to the cases were issued on the days of the operations. The details of these cases were summarized as follows:

Case No.	Products concerned	Drug ingredients	Indications	Locations
1.	VietaMas Super Calcium (超能鈣)	Vitamin D	Used as a nutritional supplement.	To Kwa Wan
2.	GNC Glucosamine 750 / Chondroitin 600, Blackmores Joint Formula etc	Glucosamine	Indicated for joint pain.	Tsuen Wan, Tsim Sha Tsui
3.	C 24/7 Natura-Ceuticals, Complete Phyto-energizer, Whitelight, and Perfect White	Vitamins	Commonly used as nutritional supplements.	Central

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.

Drug Incident

A product containing any drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. Part I poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part I poisons and unregistered pharmaceutical products are offences under the Pharmacy and Poisons Ordinance (Cap 138). The maximum penalty is a fine of $100,000 and two years' imprisonment for each offence.

Pharmacy raided for illegal sale of prescription medicine

On 15 April 2013, a joint operation was conducted by DH and the Police against a registered pharmacy resulting in the arrest of a 51-year-old salesman for suspected illegal sale of prescription medicine.

Through DH's surveillance programme, the pharmacy was found to be selling a prescription medicine without a doctor's prescription. The prescription medicine concerned contains prednisolone. It should only be sold at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription. Prednisolone is a steroidal medicine commonly used for the treatment of inflammatory diseases. Side effects include gastrointestinal discomfort, osteoporosis and Cushing's syndrome.

Members of the public were urged not to use prescription medicines on their own without advice from a doctor. Self-medication could affect treatment results and cause harmful side effects.

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: 2186 9845

E-mail: adr@dh.gov.hk

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

Post: ***Pharmacovigilance Unit,***
Drug Office, Department of Health,
Rm 1856, 18/F, Wu Chung House,
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The purpose of Drug News is to provide healthcare professionals with a summary of local and overseas drug safety news released. Healthcare professionals are advised to keep update with the information and provide corresponding advice or therapeutic measure to patients and public.