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 in the previous month. For the latest news and information, please refer to public announcements or the website of the Pharmaceutical Service of the Department of Health (http://www.psdh.gov.hk).

Safety Update

China: SFDA and Ministry of Health restricted the use of rosiglitazone and related preparations

19 October 2010 - The State Food and Drug Administration and Ministry of Health of China (SFDA) requested healthcare settings of all level should have tightened control in the use of rosiglitazone and preparations containing the drug. Rosiglitazone is a thiazolidinedione indicated for the treatment of Type II diabetes. For diabetic patients who have never used rosiglitazone or related preparations, they should start the medicine only if other oral hypoglycemic drugs are contraindicated or cannot achieve the desired blood glucose level. For users of rosiglitazone or related preparations, the cardiovascular risk should be assessed. The medicine should be used only after considering the risk-benefit balance.

In Hong Kong, the Registration Committee of the Pharmacy and Poisons Board has decided that rosiglitazone should not be used in all patients with heart failure, or history of heart failure, and that rosiglitazone should only be used in patients with Type II diabetes who cannot control their diabetes on other medications. More information on actions taken by other countries as regards the drug was reported in Drug News No. 12.

Canada: Updated safety information for the use of Innohep (tinzaparin sodium) in elderly patients with renal impairment – the IRIS clinical trial

20 October 2010 - Health Canada endorsed the safety information announced from LEO Pharma that, based on the results from a clinical study that was stopped pre-maturely, Innohep (tinzaparin sodium) is not recommended to be used on elderly patients over 70 years of age with renal impairment. Furthermore, it is recommended that the drug should be used with cautions in patients with moderate to severe renal impairment; and in all cases of impaired renal function, patients should be closely monitored. The Innohep in Renal Insufficiency Study (IRIS) which involved the use of Innohep for the treatment of acute venous thromboembolism in elderly patients with renal impairment. The IRIS was stopped prematurely as it observed that all-cause mortality in Innohep users was increased compared to patients using unfractionated heparin. The Canadian Product Monograph (CPM) has been revised to include this update safety information.

In Hong Kong, six Innohep products with different strength/packing have been registered. Tinzaparin, which is a prescription medicine, is a low molecular weight heparin indicated for the treatment of deep vein thrombosis, prevention of post-op deep vein thrombosis in patients undergoing general and orthopaedic surgery, prevention of clotting in in-dwelling IV lines for extracorporeal circulation and haemodialysis. The package insert was being updated to include the following:

- Precaution is recommended in the treatment of elderly patients with renal impairment.
- Renal function should be assessed and in patients with severe renal impairment (creatinine clearance $<$ 30ml/min), monitoring of an anti-factor Xa activity should be considered.

The United States: Change of label of GnRH agonists: (Update)

21 October 2010 – The U.S. Food and Drug Administration (FDA) announced that Gonadotropin-Releasing Hormone (GnRH) agonists

would have new safety information added to the *Warnings and Precautions* section of the drug labels. This new information warned about increased risk of diabetes and certain cardiovascular diseases (heart attack, sudden cardiac death, stroke) in men receiving these medications for the treatment of prostate cancer. GnRH agonists are approved as palliative treatement for advanced prostate cancer. FDA's decision was based on the Agency's review of several published studies. Most of these studies reported small but statistically significant increased risks of diabetes and/or cardiovascular events in patients receiving GnRH agonists. It was also reported in Drug News Issue 7 regarding the safety review of the drugs.

In Hong Kong, there are 11 registered products containing GnRH which includes goserelin, triptorelin and leuprorelin. All these products are prescription drug. Department of Health has issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about this issue. In addition, Department of Health remains vigilant to any actions of other health authorities. The issue was considered by Registration Committee of Pharmacy and Poisons Board at its meeting held on 29 December 2010 and the Committee decided that the package inserts of the products containing GnRH should include warnings relating to the increased risk of diabetes and certain cardiovascular diseases (heart attack, sudden cardiac death, stroke) in men receiving these medications for the treatment of prostate cancer.

New drug information of Invirase

22 October 2010 - The U.S. FDA announced that the label for the HIV antiviral drug Invirase (saquinavir) has been updated to describe its potentially life-threatening side effects on heart when used with Norvir (ritonavir), another HIV antiviral medication. The details of the risk was reported in Drug News Issue No. 5 in February 2010. This new risk information had been added to the *Warnings and Precautions, Contraindications, and Clinical Pharmacology* sections of the Invirase label. In addition, the FDA would require that a medication guide to be given to patients when picking up a prescription for Invirase. The medication guide would include information on the risk of abnormal heart rhythms.

The European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has recommended contraindication for use of Invirase in patients with high risk of arrthymias and patients using other medicines that may cause QT or PR prolongation. Further to this, the CHMP reviewed all available data on Invirase (saquinavir) and the potential risk of arrhythmia, and concluded that the benefit of the medicine continues to outweigh its risks. However, it is noted that the risk of QT and PR interval prolongation is dose dependent and is expected to be highest in treatment -naïve patients starting Invirase therapy. As a precautionary measure, the CHMP has recommended that treatment-naïve patients should take a reduced dose of Invirase during the first week of treatment.

On 3 November 2010, Health Canada endorsed the updates to Canadian Product Monograph (CPM) for Invirase. Additional cautionary language has been provided in the CPM to strengthen the warnings regarding QT/PR interval prolongation and to stress the need for electrocardiogram (ECG) monitoring in the treatment of HIV-infected patients with ritonavir -boosted Invirase.

In Hong Kong, two products of Invirase have been registered by Roche Hong Kong Limited and both are prescription drugs. The package inserts were updated to include the new safety information. Department of Health has issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about this new drug information.

European Union: EMA recommended use of fibrates as second-line treatment

25 October 2010 - The CHMP of EMA concluded that the benefits of the four fibrates bezafibrate, ciprofibrate, fenofibrate and gemfibrozil continues to outweigh their risks in the treatment of patients with blood lipid disorders. However, doctors should not prescribe them to newly-diagnosed patients with blood lipid disorders as first-line treatment, except for patients with severe hypertriglyceridaemia or patients who cannot take statins.

In Hong Kong, there are 51 registered products containing fibrates which include bezafibrate, ciprofibrate, fenofibrate and gemfibrozil. All these products are prescription drugs indicated for treatment of hyperlipidemia. Department of Health has issued a "Dear Healthcare Professionals" letter

to inform healthcare professionals about this issue. In addition, Department of Health remains vigilant to any actions from other health authorities. The issue on the use of fibrates as second-line treatment was considered by the Registration Committee of the Pharmacy and Poisons Board at its meeting held on 29 December 2010 and the Committee made the decision that it should be left to the physicians' clinical judgement on when to prescribe fibrates.

United Kingdom & Canada: GlucaGen Hypokit

29 October 2010 - Medicines and Healthcare products Regulatory Agency (MHRA) released class 4 drug alert (caution in use) for GlucaGen Hypokit. Novo Nordisk A/S has informed MHRA that in an extremely small number of cases, the glass of the powder vial was cracked close to the base so that when the solvent was added, the vial leaked. Use of a cracked vial may result in glucagon fluid leakage and may make the product unusable, which could result in treatment delays if no back-up kit is readily available, and potential health risks. Investigations to date suggested that the defect rate was very low, approximately 0.013%, which equated to an expected total of 2 affected vials on the UK market. Recipients of the batches YW60411 (expiry date: 31/12/2012) and YW60452 (expiry date: 31/12/2012) were asked to check their stock for signs of this defect, which was very obvious, and to discard any affected vials. Distribution of these batches has ceased and stock from alternative batches was available.

On the same day, Health Canada informed Canadians that Novo Nordisk Canada Inc. was voluntarily recalling one lot (YW60462) of the GlucaGen Hypokit after the same quality issue described above was identified that may affect a small number of kits in the affected lot. This recall was in addition to the two lots recalled in August due to a separate manufacturing concern. The recall initiated in August was reported in Drug News Issue No. 11.

In Hong Kong, GlucaGen Hypokit is registered by Novo Nordisk Hong Kong Ltd. and is a prescription drug. According to the company, the affected batches in United Kingdom and Canada have not been imported into Hong Kong.

The United States: Heparin Sodium (B. Braun): Recall - trace contaminant

1 November 2010 - B. Braun Medical Inc. and the U.S. Food and Drug Administration notified healthcare professionals of a voluntary recall of seven lots of heparin injection products to the healthcare provider level. These lots were manufactured in 2008 and would expire on 31 October 2010 and 30 November 2010. The recall is initiated in relation to a nationwide recall of certain lots of Heparin Sodium USP Active Pharmaceutical Ingredient (API) sold to B. Braun because testing indicated a trace amount of oversulfated chondroitin sulfate (OSCS) contaminant. B. Braun has not received any reports of adverse events regarding the B. Braun finished products manufactured using this API.

In Hong Kong, there is one preparation of heparin sodium registered by B. Braun Medical (HK) Limited (B. Braun). Heparin is an anticoagulant used in the treatment and prophylaxis of thromboembolic disorders. It was confirmed by B. Braun that the affected products have not been imported into Hong Kong.

China: SFDA requested the cessation of manufacturing, sale and use of sibutramine

1 November 2010 –SFDA worked with relevant experts in the assessment of the safety issue of sibutramine in China. With reference to research findings and actions taking in other countries, SFDA considered that the use of sibutramine might increase the risk of serious cardiovascular disease, and the benefit of weight loss no longer outweighed the risk. SFDA therefore decided to stop manufacturing, sale and use of sibutramine products and raw materials. All of the products containing sibutramine in the market would be recalled by the manufacturers for disposal.

On 8 October 2010, Abbott Lab Limited recalled and voluntarily cancelled the registration of two sibutramine containing products, Reductil and Sibutril in Hong Kong. On 3 November 2010, the Department of Health announced that all pharmaceutical products containing sibutramine were de-registered as recommended by the Registration Committee of the Pharmacy and

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Poisons Board. More information on actions taken by other countries as regards to the drug was reported in Drug News No. 12.

Australia: Urgent consumer level recall of APO-Perindopril 2MG tablets – blister packs of 30 tablets

9 November 2010 - The Therapeutic Goods Administration (TGA) notified consumers that Apotex Pty Ltd was undertaking an urgent consumer level recall of specified batches of APO-Perindopril 2mg tablets in blister packs of 30 tablets.This action was taken because some cartons of APO-Perindopril 2mg tablets might contain 8mg tablets. The affected batches were 24967, 24979, 25180 and 25184.

In Hong Kong, APO-Perindopril 2mg tablets is a registered prescription drug used for treatment of hypertension. The local registration certificate holder, Hind Wing Co. Ltd., confirmed that APO-Perindopril 2mg tablets has not been imported into Hong Kong.

Drug Recall

Recall of 44 batches of 39 pharmaceutical products registered by Neochem Pharmaceutical Laboratories Ltd.

On 22 October 2010, the Department of Health (DH) instructed Neochem Pharmaceutical Laboratories Ltd (Neochem), a licensed drug manufacturer, to recall from the market 42 batches of 37 registered products as they were produced when the plant was not licensed to manufacture. Following subsequent investigation, DH further instructed Neochem to recall two more products, namely Chlordiazepoxide 2.5mg Capsule (HK-27469, Batch No. 100492) and Chlordiazepoxide 10mg Capsule (HK-27481, Batch No. 100493), which are prescription medicines used for anxiety.

Between March and July 2010, Neochem recalled five products from the local market on four occasions because all were found to have insufficient active ingredients. Subsequently, the Pharmacy and Poisons (Manufacturers Licensing) Committee (the Committee) of the Pharmacy and Poisons Board suspended Neochem's manufacturer licence in April 2010. The licence was fully restored in September after the Committee was satisfied that Neochem had been in compliance with Good Manufacturing Practices (GMP).

However, through its surveillance system during the period, DH found that Neochem had actually produced between July and August, without licence, 44 batches of 39 registered products. As such, the safety, efficacy and quality of the products cannot be guaranteed. Hence, DH instructed the recall. Products under recall were listed out at the following website

http://www.dh.gov.hk/english/press/2010/101022-2.pdf

Recall of Bicolax tablet 5mg (HK-05074)

On 26 October 2010, the Department of Health (DH) instructed Synco (HK) Limited, a licensed drug manufacturer, to recall a batch of Bicolax Tablet 5mg (Batch No. 08013004(1)) as the product was found to have failed to comply with the approved specifications in Singapore. The finding came to light as a result of the department's pharmacovigilance activities that the Health Sciences Authority (HSA), the drug regulatory authority of Singapore, announced a recall of the affected batch of the product.

As the quality of the product was not guaranteed, DH ordered a recall of the affected batch in Hong Kong as a precautionary measure. In Hong Kong, the product is an over-the-counter medicine used as a laxative. The affected batch was supplied to Hospital Authority, private doctors and drug stores.

Recall of Madame Pearl's Cough Syrup N10 (HK-59222) and Madame Pearl's Cough Syrup N10 (Caramel Flavour) (HK -59221)

On 3 November 2010, the Department of Health (DH) announced that a licensed drug manufacturer, Karen Laboratories, initiated a recall of all batches of two pharmaceutical products, namely Madame Pearl's Cough Syrup N10 (Caramel Flavour) and Madame Pearl's Cough Syrup N10, from the market, in order to facilitate the Department's investigation into a complaint.

The DH received a complaint through its established vigilance system on November 1 regarding the presence of glass fragments in a bottle of Madame Pearl's Cough Syrup N10 (Caramel Flavour). Both of the above products were first registered in February this year. Both are over-the-counter

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medicines and used for the management of cough and cold.

A total of 16 batches, comprising seven of Caramel Flavour and nine of plain N10, were manufactured by Karen Laboratories and supplied to local pharmacies and medicine shops. They were also shipped to Macao. The medicines' distributor, Luxembourg Medicine Co., Ltd, has set up a hotline for public enquiries and set out details of the recall's arrangements.

Members of the public who have purchased any of the affected products are advised not to consume it and consult healthcare professionals if in doubt or feeling unwell after using the products.

Drug Incidents

Warning about Slimming Product

Public urged not to consume unlabelled slimming products from the Internet

On 18 October 2010, the Department of Health (DH) again appealed the public not to buy or use unlabelled slimming products from the internet as they may contain undeclared western medicines which may be dangerous to health. The appeal followed arrest of a 22-year-old woman in a DH's joint operation with the Police on the same day for suspected illegal sale of pharmaceutical products. A number of suspected unregistered pharmaceutical products were also seized from the woman at the time of her arrest.

Acting on intelligence relating to suspected illegal sale of slimming products via the Internet allegedly obtained from a hospital in Thailand, DH obtained the slimming products through the Internet and sent them to Government Laboratory for analysis. Test results showed that two slimming drugs contained western medicines. In one of the slimming drugs, a prescription medicine, sibutramine, was found while the other was found to have contained an over-the-counter laxative, bisacodyl.

Public urged not to buy a slimming product, “Crystal Pills”, with undeclared Western drug ingredients

On 27 October 2010, the Department of Health (DH) advised members of the public not to buy or use a slimming product named “Crystal Pills”, as it was found to have contained undeclared western drug ingredients that may be dangerous to health. The product was obtained from the Internet via the DH's surveillance programme. Laboratory analysis results released on the same day showed the presence of western drug ingredients sibutramine and its analogue in the product.

A joint operation was conducted by DH and the Police on the same day, resulting in the arrest of a 55 -year-old woman for suspected illegal sale of unregistered pharmaceutical products. During the operation, a number of other suspected unregistered pharmaceutical products were also seized from the woman.

Sibutramine was once used for treatment of obesity. Products containing sibutramine has been banned since November 2010 for its risk of serious cardiovascular side-effects. Sibutramine analogues, being chemically similar to sibutramine, are expected to have the same side effect as sibutramine.

Bisacodyl is a western medicine used as a stimulant laxative. Its side effects include abdominal discomfort such as colic or cramps. Prolonged use or overdosage can result in diarrhea with excessive loss of water and electrolytes. There is also the possibility of developing an atonic non-functioning colon. Products containing bisacodyl is an over-the-counter product.

Warning about other products

Recall of "An Chuang San Ri Qing (Xian Tao Lu)" [暗瘡三日清（仙桃露）]

On 8 November 2010, the Department of Health (DH) called on members of the public not to buy or use a product labelled as "An Chuang San Ri Qing (Xian Tao Lu)" as it was found to have contained an undeclared western medicine, metronidazole. The appeal was made following DH's market surveillance under its established vigilance system which aims to scan for possibly adulterated consumer products with health claims. According to the wholesaler of the product, Lee Sze Trading Company (a licensed proprietary Chinese medicine wholesaler), the product was imported from the Mainland for sale in Hong Kong. The wholesaler was instructed to immediately recall the product and they have set up a hotline to answer public enquiries.

Metronidazole is a western medicine for treating anaerobic and protozoal infections. Its side effects include gastrointestinal disturbances, especially

nausea and an unpleasant metallic taste. Products containing metronidazole are Part I poisons and can be sold only under the supervision of a pharmacist.

Recall of "Once OK Beriberi Lotion" [華陀一搽靈]

On 9 November 2010, DH called on members of the public not to buy or use a topical product labelled as "Once OK Beriberi Lotion" as it was found to contain an undeclared western medicine, benzoic acid, a drug used in treating fungal infections. The appeal was made following DH's market surveillance under its established vigilance system which aims to scan for possibly adulterated consumer products with health claims. The product was manufactured in Hong Kong by licensed Chinese medicine manufacturer, Hong Kong Chung Shun Medicine Manufactory, and distributed by Wah Fai Hong, a licensed Chinese medicine wholesaler. The wholesaler was instructed to immediately recall the product and set up a hotline to answer public enquiries.

The side effects in topical use of Benzoic acid include hypersensitivity reactions. Products containing benzoic acid are over-the-counter products.

The aforementioned products were not registered pharmaceutical products under the Pharmacy and Poisons Ordinance in Hong Kong. A product containing any western drug ingredient must be registered under the Ordinance before it can be sold in Hong Kong. Under the Pharmacy and Poisons Ordinance, possession or sale of unregistered pharmaceutical product is an offence liable to the maximum penalties of a $100,000 fine and two year's imprisonment.

Members of the public should stop using the aforementioned products that contained undeclared western drug ingredients and they should see doctors if they feel unwell after using the products.

Useful Contact

Drug Complaint:

Tel: 2572 2068

Fax: 2147 0457 & 2123 1996

E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

You are encouraged to report any suspected or confirmed ADR cases to our office by:

Fax: 2147 0457

E-mail: adr@dh.gov.hk

Post: ***ADR Monitoring Unit,***

Pharmaceutical Service, Department of Health,

3/F, Public Health Laboratory Centre,

382 Nam Cheong Street, Kowloon