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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

US Food and Drug Administration announced new safety controls for long-acting beta agonists, medications used to treat asthma

18 February 2010 - Due to safety concerns, the US Food and Drug Administration (FDA) had required changes to Long-Acting Beta-Agonists (LABAs) which are used in the treatment of asthma. These changes were based on FDA's analyses of studies showing an increased risk of severe exacerbation of asthma symptoms, leading to hospitalizations in pediatric and adult patients as well as death in some patients using LABAs.

To ensure the safe use of these products, LABAs should not be used alone, they should only be used in combination with an asthma controller medication. To ensure compliance with both medications in pediatric and adolescent patients, they should use a combination product containing both an inhaled corticosteroid and a LABA. LABAs should only be used long-term in patients whose asthma cannot be adequately controlled on asthma controller medications. LABAs should be used for the shortest duration of time required to achieve control of asthma symptoms and discontinued, if possible, once asthma control is achieved. Manufacturers had been required to include this information in the product labels of these drugs, along with taking other steps to reduce the overall use of these medications.

In Hong Kong, long-acting beta agonists containing salmeterol or formoterol are available. They are prescription medicines.

There are single-ingredient products and combination products with corticosteroid. The single-ingredient products are indicated to be used with corticosteroid. The Registration Committee of the Pharmacy and Poisons Board has reviewed the above safety concerns and decided that warning statement as regards the above safety information should be included in the sales pack labels or product inserts of all these products.

US Food and Drug Administration notified healthcare professionals about changes in the prescribing information for Exjade (deferasirox)

18 February 2010 - Novartis Oncology and FDA notified healthcare professionals about recent changes in the prescribing information for Exjade, indicated for the treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older. It includes information that the product may cause renal impairment, including failure, hepatic impairment, including failure and gastrointestinal hemorrhage. In some reported cases, these reactions were fatal. These reactions were more frequently observed in patients with advanced age, high risk myelodysplastic syndromes, underlying renal or hepatic impairment or low platelet counts. Exjade therapy requires close patient monitoring, including measurement of serum creatinine and/or creatinine clearance, serum transaminases and bilirubin.

In Hong Kong, Exjade is registered by Novartis Pharmaceuticals (HK) Ltd. It is a prescription

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medicine. Changes regarding the above safety information have been made in the package insert of Exjade.

Ongoing safety review of Invirase (saquinavir) and possible association with abnormal heart rhythms by US Food and Drug Administration

23 February 2010 - US Food and Drug Administration (FDA) notified healthcare professionals and patients that it is reviewing clinical trial data about a potentially serious effect on the heart from the use of Invirase (saquinavir) in combination with Norvir (ritonavir), antiviral medications given together to treat HIV infection.

The data suggested that together the two drugs may affect the electrical activity of the heart, known as prolonged QT or PR intervals. A prolonged QT interval can increase the risk for a serious abnormal rhythm called torsades de pointes. A prolonged PR interval can cause the electrical signal responsible for generating a heart beat to slow or even stop, known as heart block. FDA's analysis of these data is ongoing, the agency will update the public as soon as this review is complete. However, healthcare professionals should be aware of this potential risk for changes to the electrical activity of the heart.

In Hong Kong, Invirase and Norvir are registered by Roche Hong Kong Ltd and Abbott Lab. Ltd. respectively. Both of them are prescription medicines. A "Dear Healthcare Professionals" letter has been issued to alert healthcare professionals about this potential risk for changes to the electrical activity of the heart.

Risk of intravascular hemolysis associated with WinRho SDF (Rho(D) Immune Globulin Intravenous (Human)) reported by US Food and Drug Administration

10 March 2010 - Cangene, Baxter and US Food and Drug Administration (FDA) notified

healthcare professionals that cases of intravascular hemolysis (IVH) and its complications, including fatalities, have been reported in patients treated for immune thrombocytopenic purpura (ITP) with WinRho SDF. IVH can lead to clinically compromising anemia and multi-system organ failure including acute respiratory distress syndrome. Serious complications including severe anemia, acute renal insufficiency, renal failure and disseminated intravascular coagulation had also been reported. Fatal outcomes associated with IVH and its complications had occurred most frequently in patients of advanced age (age over 65) with co-morbid conditions. The company had added a "Boxed Warning" to the labeling for the product which strengthens the warnings related to the risk of developing IVH in the ITP population.

In Hong Kong, WinRho SDF is registered by Hind Wing Co Ltd. This safety information has been included in the package insert of WinRho SDF

New changes to the dose conversion guidelines for Fentanyl Transdermal Systems in Canada

10 March 2010 - The manufacturers of Fentanyl Transdermal Systems (FTS) in collaboration with Health Canada informed healthcare professionals of important new information regarding changes to the Dose Conversion Guidelines. A 1:3 parenteral to oral morphine dose ratio replaces the previous 1:2 parenteral to oral morphine dose ratio, (e.g. 10mg parenteral morphine = 30mg oral morphine). The conversion doses of IV/IM morphine to Fentanyl Transdermal Systems for the 75, 87 and 100mcg/hour patch strengths were revised to 'not applicable' to reflect the insufficiency of data available for guidance. Fentanyl is a very strong opioid narcotic pain medicine that can cause serious and life-threatening breathing problems if the dosage used is too high. Manufacturers of all fentanyl transdermal patches are working with Health Canada to

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include this safety information in the Dosing and Administration section in all Canadian Product Monographs for Fentanyl Transdermal Systems.

In Hong Kong, there are two brands of fentanyl transdermal products, “Durogesic” and “Fentanyl HPQ” which are registered by Johnson and Johnson (Hong Kong) Ltd and IDS (Hong Kong) Limited – Healthcare Division respectively. They are both prescription medicines. The above change has been made in the package insert of “Durogesic”. For “Fentanyl HPQ”, its dosage is following the regimen currently used in European Union countries.

Reduced effectiveness of Plavix (clopidogrel) in patients who are poor metabolizers of the drug by US Food and Drug Administration

12 March 2010 - The US Food and Drug Administration (FDA) added a boxed warning to the anti-blood clotting drug Plavix (clopidogrel), alerting patients and health care professionals that the drug can be less effective in people who

cannot metabolize the drug to convert it to its active form. Plavix reduces the risk of heart attack, unstable angina, stroke, and cardiovascular death in patients with cardiovascular disease by making platelets less likely to form blood clots. Plavix does not have its anti-platelet effects until it is metabolized into its active form by the liver enzyme, CYP2C19. People who have reduced functioning of their CYP2C19 liver enzyme cannot effectively convert Plavix to its active form. As a result, Plavix may be less effective in altering platelet activity in those people. These “poor metabolizers” may not receive the full benefit of Plavix treatment and may remain at risk for heart attack, stroke, and cardiovascular death.

Plavix and other products containing clopidogrel are available in Hong Kong. They are prescription medicines. Plavix is registered by Sanofi-Aventis Hong Kong Limited, and its package insert regarding the above safety information has been updated. The Registration Committee of the Pharmacy and Poisons Board has reviewed the issue and decided that warning statement as regards the above safety information should be included in sales pack labels or product inserts of the products accordingly.

Drug Recall

Recall of pharmaceutical product — PMS-Carvedilol 12.5mg Tablets (HK-52639)

On 19 February 2010, Trenton-Boma Limited, a licensed wholesaler of pharmaceutical products, initiated a recall of one of PMS-Carvedilol 12.5mg tablets (Batch No. 44437).

The product is manufactured in Canada. It is a prescription medicine used for the treatment of high blood pressure and heart failure. A total of 2,218 bottles (100 tablets per bottle) of the batch had been supplied to the Hospital

Authority, and 71 bottles to some private doctors and pharmacies.

It was revealed that, on some of the bottles of the product, the additional label that the wholesaler had added in order to comply with the local statutory labeling requirements, stated incorrectly that each tablet contained 6.25mg carvedilol and showed an incorrect registration number.

The wholesaler initiated a recall exercise at retail level. It also set up a hotline to answer clients' enquiries.

Drug Incident

Warning about Slimming Products

Public urged not to consume slimming product “S&S Super Slender” with undeclared drug ingredients

On 25 February 2010, people were urged not to buy or consume a slimming product “S&S Super Slender 燃脂膠囊” as it was found to have contained undeclared western medicine that may cause serious side effects.

Laboratory results on two samples of the product showed that both contained a sibutramine analogue, and one of them also contained phenolphthalein and sibutramine. The product was offered for sale on an internet auction website as a package of “S&S Super Slender 燃脂排油減肥套盒” containing either in a 120-capsule bottle or 60 two-capsule packs of “S&S Super Slender 燃脂膠囊”.

Public urged not to consume slimming product “Marsha Slim Plus” with undeclared drug ingredients

On 4 March 2010, members of the public were urged not to buy or consume a slimming product named “Marsha Slim Plus” as it was found to have contained undeclared western drug ingredients that may cause serious side effects.

Product samples were obtained in a shop in Mongkok. Laboratory results showed the presence of sibutramine and its analogue, as well as phenolphthalein.

The product was offered for sale in “Marsha Health Care Formula 瑪沙醫學美容補身美肌配方” and each pack of the product contained a 60-capsule bottle of “Marsha Slim Plus” and 30 “Marsha” teabags.

The Department of Health mounted an operation on 4 March 2010, resulting in the seizure of 27 bottles of the above product. A 64-year-old woman was arrested during the operation.

Man arrested for selling slimming product “Comecoo” with undeclared drug ingredients

On 8 March 2010, a 26-year-old man was arrested in a joint operation between the Department of Health and the police as part of a follow-up investigation into the sale of an unregistered slimming product which was earlier found to have contained undeclared western drug ingredients.

The man was suspected of selling the product named “Comecoo 康美柯—完美自我”. Two boxes of the product were seized from the man at the time of his arrest and four boxes of “Comecoo” were also found in a home search.

According to preliminary enquiry, it was claimed that the product was obtained from the Mainland.

Late in 2009, the department obtained “Comecoo” from an Internet auction website during the department’s surveillance operation. The department issued a warning in December 2009 reminding people not to take the product as laboratory tests on the product showed the presence of sibutramine, phenolphthalein and two analogues of sibutramine.

Woman arrested for selling slimming product “Zhongcaoyao-Jiankangjianfei” with undeclared drug ingredients

On 12 March 2010, a 49-year-old woman was arrested in a joint operation between the Department of Health and the police as part of a follow-up investigation into the sale of an unregistered slimming product which was earlier found to have contained undeclared western drug ingredients.

The woman was suspected of selling the product named “Zhongcaoyao-Jiankangjianfei 中草藥—健康減肥軟膠囊”. Two boxes of the product were seized from the woman at the time of her

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arrest.

Late in 2009, the department obtained the product concerned from an Internet auction website during the department's surveillance operation. The department issued a warning in December 2009 reminding people not to take the product as laboratory tests on the product showed the presence of sibutramine and its analogues.

Sibutramine is a western medicine used as an appetite suppressant. Its side effects include increased blood pressure and heart rate, psychosis and possibly convulsion. People with heart problems

should not take it. Products containing sibutramine can be sold only on a doctor's prescription and dispensed under the supervision of a pharmacist. Sibutramine analogues, being chemically similar to sibutramine, are expected to have the same side effect as sibutramine. Phenolphthalein was once used for treating constipation but has been banned for its cancer-causing effect.

Weight control should be achieved through good diet and appropriate exercise. People should consult healthcare professionals before using any medication for weight control.

Warning about Other Products

Woman arrested for selling unregistered pharmaceutical product “Tai Er Si Yi Wei A Suan Jiao Wan” on the Internet

On 2 March 2010, a 42-year-old woman was arrested in a joint operation between the Department of Health and the Police as part of a follow-up investigation into the sale on the internet of a product which claimed to contain a western medicine, isotretinoin.

The woman, suspected of selling and possessing an unregistered pharmaceutical product, was arrested for investigation. A number of boxes of the product “Tai Er Si Yi Wei A Suan Jiao Wan 泰爾絲異維 A 酸膠丸” were found in a home search.

Investigation revealed that the products were obtained from a Mainland drug store and put up for sale on an auction website. The department issued a warning on 12.2.2010 reminding people not to use the product as it claimed to contain isotretinoin.

Isotretinoin is a western medicine. Taken orally, it is used for treating severe acne that has not responded to other treatments. The medicine is not indicated for uncomplicated adolescent acne. Its common side effects include dryness of skin with scaling and redness, conjunctivitis, dry sore mouth, visual disturbance, hair thinning and mood changes. It

may cause foetal malformation and spontaneous abortion and should not be used during pregnancy. Pregnancy should be avoided for one month after treatment has been stopped.

Products containing isotretinoin can be sold only on a doctor's prescription and dispensed under the supervision of a pharmacist

Those with skin problems should consult medical professionals for appropriate advice and treatment.

All of 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 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.

The Department of Health had stepped up joint efforts with the Police against the illegal sale of pharmaceutical products on the internet. Members of the public were exhorted not to sell products of unknown or doubtful composition. Members of the public should stop using the aforementioned products and they should see doctors if they feel unwell after taking the products. They should destroy and dispose of the aforementioned products or submit them to the Department's Pharmaceutical Service during office hours.

Drug Incident

Only licensed dispensaries authorised to sell prescription drugs

On 10 March 2010, the Department of Health launched an investigation upon receipt of media enquires about two drug distributors sold four prescription drugs, Aranesp, Recormon, Mircera and Renagel, directly to kidney patients.

Aranesp, Recormon and Mircera are registered medicines for treating patients with anaemia associated with chronic renal failure whereas Renagel is a registered medicine used for hyperphosphataemia in patients with chronic renal failure.

On 11 March 2010, further investigation of department of health revealed that four more prescription drugs, namely CellCept, Eprex, Pegasys and Regpara were also sold by their wholesalers directly to their patients.

Eprex and Regpara are both usually used by patients with chronic renal failure, the former for management of anaemia and the latter for treatment of secondary hyperparathyroidism. CellCept is used as an immunosuppressant for the prevention of graft rejection while Pegasys is used by patients with hepatitis.

CellCept, Eprex, Pegasys and Regpara are all registered in Hong Kong by three wholesalers. Two of which had already been revealed by previous investigation and there was another one revealed on the investigation of 11.3.2010.

Taken together, investigation thus far revealed that a total of eight prescription drugs, three wholesalers, 14 Hospital Authority hospitals and four private hospitals were involved. The hospitals were Alice Ho Miu Ling Nethersole Hospital, Caritas Medical Centre, Kwong Wah Hospital, North District Hospital, Pamela Youde Nethersole Eastern Hospital, Prince of Wales Hospital, Princess Margaret Hospital, Queen Elizabeth Hospital, Queen Mary Hospital, Tuen Mun Hospital, Tung Wah Hospital, United Christian Hospital, Wong Tai Sin Hospital and Yan Chai Hospital; and in the

private sector, Baptist Hospital, Canossa Hospital, St Paul's Hospital and St Teresa's Hospital.

Investigation revealed that the practice in question probably commenced around 2004 at the earliest. It was understood that two modes of operation were used.

In the first mode adopted by one wholesaler, the drugs were sold directly to patients who had prescriptions, bypassing licensed dispensaries.

In the second mode adopted by the other two wholesalers, patients placed orders with the wholesalers directly. The drugs were then delivered to patients through distributors which also collected the prescriptions and money and sent the former to licensed dispensaries.

It was apparent that both modes were enabled through hospital healthcare workers who introduced the wholesalers to patients besides supplying them with the prescriptions. Investigation is ongoing.

All 8 prescription drugs can be sold only on a doctor's prescription and dispensed under the supervision of a pharmacist. According to the Pharmacy and Poisons Ordinance (Chapter 138), only licensed dispensaries are authorised to sell prescription drugs to patients. Sale of controlled drugs by any company or anybody not in accordance with the law is an offence under the Ordinance. The maximum penalty is a fine of \$100,000 and two years' imprisonment.

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: 2572 4570 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