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

Calcium gluconate 10% in 10 mL glass containers: Risk of aluminium exposure

16 September 2010 – A UK review of scientific evidence had concluded that calcium gluconate injection (10%) solution packed in 10mL glass containers contained high aluminium levels which could cause adverse effects on healthy bone maintenance and brain and nerve development, particularly in patients with kidney problems, or in children. Therefore, calcium gluconate in 10mL glass containers should no longer be used for prolonged or repeated treatment in these groups of patients; calcium gluconate injection packed in plastic containers should be used instead. Calcium gluconate is a medicine used to treat hypocalcaemia and is also used in cardiac resuscitation and for a condition in newborn babies called tetany.

Only one calcium gluconate injection is available in Hong Kong and is registered by B Braun Medical (HK) Ltd. The registered calcium gluconate injection is in plastic ampoules.

FDA issued new dosing guidance for children using Valcyte

16 September 2010 - The United States Food and Drug Administration notified health care professionals of updated dosing recommendations for Valcyte (valganciclovir) oral tables and solution used by children and adolescents received kidney or heart transplant. The update was intended to prevent drug overdosing of children with low body weight, low body surface area, and very low serum creatinine. The product's label was revised to include an upper limit on "calculated creatinine clearance" as dosing instruction. Valcyte is an antiviral agent and in US, the medication can be used for the prevention of cytomegalovirus (CMV) disease in children from 4 months to 16 years of age who have undergone a kidney or heart transplant and who are at a higher risk of getting the disease.

In Hong Kong, only Valcyte Tablet is registered by Roche Hong Kong Ltd. It is not indicated for use in children and adolescents.

Risk of fatal anaphylaxis associated with Actemra (tocilizumab)

20 September 2010 – Further to the same alert of August 2010 reported in Issue No. 11 of Drug News, Hoffmann-La Roche Limited, in consultation with Health Canada, also informed healthcare professionals in Canada of the important safety information regarding Actemra (tocilizumab) and anaphylaxis. Actemra is an intravenous drug mainly used in combination with methotrexate for the treatment of moderate and severe active rheumatoid arthritis. Healthcare professionals were advised to closely monitor patients during and after Actemra infusion and to stop the infusion and administer appropriate therapies if a reaction occurs. Please refer to Drug News Issue No. 11 for further details.

In Hong Kong, Actemra is registered by Roche Hong Kong Ltd, and its package insert has been updated regarding this safety issue. In response to the notification informed by Roche in August 2010, the Department of Health has issued a press statement and a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information.

Ongoing safety review on Actos (pioglitazone) by the FDA

20 September 2010 - The United States Food and Drug Administration (FDA) announced that it had begun a safety review of the diabetes drug Actos (pioglitazone), after receiving preliminary five-year

data from a an ongoing 10-year observational cohort study conducted by the manufacturer, Takeda Pharmaceuticals North America Inc., San Diego. The study was designed to evaluate the risk of bladder cancer associated with use of this drug. Although these early results did not show statistically significant association between Actos exposure and risk of bladder cancer, an increased risk was observed in patients with the longest exposure to Actos and in those with the highest cumulative dose of the drug. FDA was reviewing the data from this study and a case control study that was nested within it, and would update the public when the review was completed or earlier should additional data become available.

In Hong Kong, Actos is registered by Takeda Pharmaceuticals Taiwan Limited and there is a total of 22 pioglitazone-containing products registered in Hong Kong. The Department of Health remains vigilant to any new findings about pioglitazone.

European Medicines Agency confirmed positive benefit-risk balance of RotaTeq

24 September 2010 - Following a review of the oral vaccine RotaTeq, the European Medicines Agency's Committee for Medicinal Products for Human Use had concluded that the presence of a very small amount of viral DNA fragments in the vaccine did not present a risk to public health and that the vaccine continued to have a positive benefit-risk balance. The review of RotaTeq was initiated after the unexpected detection of DNA fragments of porcine circovirus (PCV) in the vaccine. Sanofi Pasteur MSD would take measure to continue to ensure that the vaccine is produced free of PCV.

In Hong Kong, Rotateq Vaccine Oral Suspension (registered by Merck Sharp & Dohme (Asia) Ltd) has been recalled in May 2010 as a precautionary measure following the discovery of PCV by the manufacturer. After a careful assessment, the Department of Health had concluded that the benefits of these vaccines outweigh the risks and resume the use of the vaccine in Hong Kong since 17 May 2010 following. The situation of rotavirus vaccine in Hong Kong has been reported in more details in Issue No. 10 of Drug News.

Restricted use of rosiglitazone products

A Europe-wide review of the risks and benefits of medicines containing rosiglitazone has concluded that the benefits of treatment no longer outweigh the risks. Rosiglitazone is a thiazolidinedione indicated for the treatment of Type II diabetes. There is increasing evidence from studies suggesting that the drug is associated with an increased risk of cardiovascular disorders, including heart attacks and heart failure. As people with diabetes are already at an increased risk of cardiovascular disease, use of rosigiltazone among diabetic patient might further increase these risks.

In Europe, the European Medicines Agency (EMA) recommended the suspension of the marketing authorization for the rosiglitazone-containing medicines in September 2010. In United States, the Food and Drug Administration (FDA) announced in the same month that it would significantly restrict the use of rosiglitazone to patients with Type II diabetes who cannot control their diabetes on other medications via a restricted access programme. In Australia and Singapore, the corresponding health authorities have also taken significant steps to restrict the use of rosiglitazone, including limiting the use of rosiglitazone to selected patients who are unable to effectively control their blood sugar with the use of other anti-diabetic medications, and not with heart failure, or history of heart failure. The details of the safety information released by United Kingdom and European Union have been reported previously in Issue No. 7 and Issue No. 10 of Drug News respectively.

In Hong Kong, products containing rosiglitazone are prescription medicines and there are a total of 17 pharmaceutical products containing rosiglitazone registered. On 4 October 2010, after careful consideration of information available and the regulatory action taken by other health authorities, the Registration Committee of the Pharmacy and Poisons Board had decided that rosiglitazone should only be used in patients with Type II diabetes who cannot control their diabetes on other medications and should not be used in patients with heart failure, or history of heart failure. The Committee also requested that the package insert of rosiglitazone products should be revised to include this safety information. The Department of Health (DH) had issued a press statement regarding the recommendation by the Registration Committee on the same date.

Lipitor recall in United States

11 October 2010 - In United States, Pfizer recalled specific bottles of Lipitor (40mg only) due to a small number of reports of an uncharacteristic odor related to the bottles in which Lipitor was packaged. Medical assessment had determined that the odor was not likely to cause adverse health consequences in patients taking Lipitor. Pfizer was working with the bottle supplier to determine the cause of the problem.

In Hong Kong, Lipitor is registered by Pfizer Corporation Hong Kong Limited as treatment for hypercholesterolemia. Only the blister package has been imported into Hong Kong market.

Oral liquid cough medicines containing codeine: should not be used in children and young people under 18 years

12 October 2010 – In UK, the Commission on Human Medicines and its Paediatric Medicines Expert Advisory Group had evaluated the benefits and risks of over-the-counter (OTC) oral liquids containing codeine for the treatment of cough in children, based on all available data. They concluded that the risks associated with OTC oral liquid cough medicines containing codeine outweigh the benefits in children and young people under 18 years and advised that:

- OTC oral liquid medicines containing codeine should no longer be used to treat cough in children and young people under 18 years.
- all over-the-counter oral liquid codeine medicines will be supplied in child-resistant containers.

The packaging and leaflets for OTC liquid cough medicines that contain codeine in UK were being updated.

There are about 330 oral liquid products containing codeine registered in Hong Kong. In April 2009, the Registration Committee of Pharmacy and Poisons Board had decided that products for the treatment of cough and cold should not be used for children under 6 years of age, and the label of cough and cold products should carry this information. In light of the new recommendation from UK, the issue will be considered by the Registration Committee of the Pharmacy and Poisons Board. Department of Health remains vigilant to any new actions of other health authorities on codeine products.

Important information regarding the quality, safety and supply of Pegtron (ribavirin capsules plus peginterferon alfa-2b in Redipen)

13 October 2010 – In Canada, Schering-Plough Canada Inc., a subsidiary of Merck & Co. Inc., informed a manufacturing defect had been observed at a low frequency in the glass stopper sealing flange at one end of the glass cartridge of Redipen in Pegetron, which might render the seal incapable of sustaining a vacuum. This defect had the potential to compromise sterility and potentially lead to contamination and injection site infection. Pegetron is indicated for the treatment of adult patients with chronic hepatitis C.

Schering-Plough Canada Inc. was experiencing supply constraints of Redipen. Merck was of the view that patients already on therapy should continue the use of Pegetron Redipen and Merck would replace the supplies at the pharmacy/retail level once the newly manufactured Redipen was available.

In Singapore, SOL Limited (Singapore Branch), a subsidiary of Merck & Co. Inc, conducted a voluntary recall of all strengths of Peg-Intron Redipen Injection as a precautionary measure in relation to the incident mentioned above. All sales of Peg-Intron Redipen Injections had been suspended and all existing stocks of all the affected batches were recalled. Until unaffected units of Peg-Intron Redipen became available, healthcare professionals were advised not to initiate Peg-Intron treatment on new patients and to consider switching existing patients to alternative therapies.

In Hong Kong, Redipen is registered as Peg-Intron by Schering-Plough Div. of SOL Limited. The products had been supplied to public and private hospitals and private practitioners. The Schering-Plough had inspected its stock as well as the stock in all the involved doctors and hospitals and no abnormality was detected. Department of Health has issued a press statement and a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information.

Update on worldwide actions on sibutramine

8 October 2010 –The Department of Health received notification from licensed drug company Abbott Lab Ltd. that the company would voluntarily withdraw the registration of Reductil and its generic version Sibutil (both containing sibutramine) in Hong Kong and recall the products from local market. Sibutramine is a serotonin and noradrenaline reuptake inhibitor that is indicated for treatment of obesity. With the concerns of cardiovascular adverse events among patients using sibutramine, the Sibutramine Cardiovascular Outcomes Trial (SCOUT) was conducted to assess these risks. The result of SCOUT showed that when compared with placebo, use of sibutramine in a high cardiovascular risk population is associated with increased risk of serious, non-fatal cardiovascular events, such as stroke or heart attack.

In Hong Kong, products containing sibutramine are prescription medicines. Other than the 2 products of Abbott Lab Ltd., there are 49 generic products containing sibutramine registered in Hong Kong. DH had issued a press statement and a "Dear Healthcare Professionals" letter regarding the withdrawal of the registration of Reductil and Sibutil and recalled the product from local market. The Registration Committee of the Pharmacy and Poisons Board considered the SCOUT study, the use of the product in Hong Kong, and the regulatory actions of other international regulatory agencies in its recent meeting held in November 2010 and decided to deregister all products containing sibutramine.

In Europe, United States, Australia, Canada and Singapore, sibutramine was withdrawn from the market by the corresponding health authorities or the manufacturers after reviewing the data from the SCOUT study.

Situation in Europe

The European Medicines Agency has completed a review of the safety and effectiveness of sibutramine. The Agency's Committee for Medicinal Products for Human Use has concluded that the benefits of sibutramine do not outweigh its risks, and that all marketing authorizations for medicines containing sibutramine should be suspended throughout Europe. The European Commission issued a decision on 6 August 2010.

Situation in United States

On 8 October 2010, the U.S. Food and Drug Administration (FDA) announced that Abbott Laboratories had agreed to voluntarily withdraw its obesity drug Meridia (sibutramine) from the U.S. market because of clinical trail data indicating an increased risk of heart attack and stroke. The FDA requested the market withdrawal after reviewing data from the SCOUT study.

Situation in Australia

Following discussion with the Therapeutic Goods Administration (TGA), Abbott Australia would cease supply of sibutramine (Reductil) in Australia from 9 October 2010.

Situation in Canada

Health Canada informed healthcare practitioners and Canadians that Abbott Laboratories was voluntarily withdrawing the prescription weight-loss drug sibutramine, which is marketed under the brand name Meridia®, from the Canadian market on 8 October 2010. On 14 October 2010, Health Canada further updated healthcare practitioners and Canadians with respect to the two generic forms of sibutramine drugs authorized in Canada, Apo-sibutramine and Novo-sibutramine Apotex Inc., the manufacturerof Apo-sibutramine, had agreed to voluntarily withdraw this drug from the Canadian market. Teva Canada Ltd., the manufacturer of Novo -sibutramine, had confirmed to Health Canada that it has not marketed drug in Canada.

Situation in Singapore

On 11 October 2010, Health Sciences Authority suspended the sales of sibutramine products in Singapore, after consulting its Pharmacovigilance Advisory Committee (PVAC) and a panel of external experts in metabolic diseases and cardiology.

Safety review of bisphosphonate drugs and the possible risk of rare but serious thigh bone factures

Situation in United States

13 October 2010 – Further to the reports of United

States (U.S.) on possible increased risk of certain types of thigh bone fractures with long-term bisphosphonates use as published in Issue No. 11 of Drug News, FDA warned patients and healthcare providers about the possible risk of atypical thigh bone (femoral) fracture in patients who take bisphosphonates. A labeling change and inclusion of a medication guide have been implemented to reflect the risk.

The labeling change and medication guide would affect only those bisphosphonates approved for osteoporosis, including oral bisphosphonates such as Fosamax, Fosamax Plus D, Actonel, Actonel with Calcium, Boniva, Atelvia, and their generic products, as well as injectable bisphophonates such as Reclast and Boniva. Labelling change and medication guide would not apply to bisphosphonates used for Paget's disease or cancer/ hypercalcemia such as Didronel, Zometa, Skelid, and their generic products.

The FDA recommended that healthcare professionals be aware of the possible risk in patients taking bisphosphonates and consider periodic reevaluation of the need for continued bisphosphonate therapy for patients who have been on bisphosphonates for longer than five years.

Situation in Canada

15 October 2010 – Health Canada also announced that they were conducting an ongoing safety review of bisphosphonates and the increased risk of atypical thigh bone fracture. Based on the scientific evidence available, Health Canada considered that the benefits of bisphosphonate outweigh the risks when used as directed in the Canadian Product Monographs. Health Canada would take action and inform health professionals and Canadians as necessary if new safety information was identified.

Situation in Hong Kong

In Hong Kong, there are a total of 56 products registered containing bisphosphonates. Out of which, 41 products, including alendronate, ibandronate, risedronate and zoledronic acid, are prescription drugs approved for osteoporosis. As reported in Drug News Issue 11, DH had issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information. DH remains vigilant to any new finding about this class of drug and the issue will be considered in the meeting of the Registration Committee of Pharmacy and Poisons Board scheduled to be held in December 2010.

Information on association of Aclasta (zoledronic acid 5mg/100mL) solution for intravenous infusion with renal dysfunction provided by Health Canada

15 October 2010 – Health Canada and Novartis Pharmaceuticals Canada Inc. provided the healthcare professionals with important renal safety information on renal dysfunction based on post-marketing experience with Aclasta. The monograph of Aclasta has been revised and Novartis would like to reinforce the current recommendations for selecting appropriate patients for Aclasta in order to minimize the risk of renal adverse reactions.

As of 30 April 2010, Novartis had received 265 spontaneous reports of renal impairment following administration of Aclasta, corresponding to a reporting rate of approximately 20 cases per 100,000 patient-years of exposure.

Therefore, the following precautions were advised to be taken to minimize the risk of renal adverse reactions:

- Aclasta should not be used in patients with severe renal impairment (creatinine clearance <30 mL/min).
- Aclasta should be used with caution when concomitantly used with other drugs that could impact renal function.
- Creatinine clearance should be calculated (e.g., Cockcroft-Gault formula) before each treatment with Aclasta followed by periodic monitoring of serum creatinine in patients with risk factors. Transient increase in serum creatinine may be greater in patients with underlying impaired renal function.
- Patients should be appropriately hydrated (500 mL or 2 glasses of water) prior to and following administration of Aclasta, especially elderly patients and those receiving diuretic therapy.
- A single dose of Aclasta should not exceed 5 mg and the duration of infusion should be no less than 15 minutes.

Safety Update

In Hong Kong, Aclasta is registered by Novartis Pharmaceuticals (HK) Limited. It is a drug indicated for treatment of osteoporosis in postmenopausal women. Department of Health (DH) had issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information. DH remains vigilant to any new finding about this drug. The issue will be considered in the meeting of the Registration Committee of Pharmacy and Poisons Board scheduled to be held in the end of December 2010.

Rhinathiol 2% (carbocisteine) – Contraindication in children below 2 years old in Singapore

15 October 2010 – In Singapore, Sanofi-Aventis Singapore Pte Ltd informed healthcare professionals that they would adopt the French authorities' decision to contraindicate the use of Rhinathiol 2% Children and Infant Syrup in children below 2 years of age. This decision arose from the French Regulatory Agency's evaluation of pharmacovigilance data indicated the risk of aggravation of respiratory symptoms in connection with the use of mucolytic products to treat bronchial secretion in children below 2 years old. The package insert for Rhinathiol 2% Children and Infant Syrup would be updated to reflect this new contraindication and the package would subsequently be renamed as Rhinathiol 2% Children Syrup.

In Hong Kong, there are 18 registered products containing carbocisteine. None of these products are recommended for age under 2 years.

Drug Recall

Recall of pharmaceutical products by Universal Pharmaceutical Laboratories Limited

On 6 October 2010, drug manufacturer Universal Pharmaceutical Laboratories Limited (Universal) recalled four batches of products namely, Uni-Zyme 30mg tablets (HK-45451) (Batch no: 10030811), Uni-Hydrin 50mg tablets (HK-35110) (Batch no: 1001004 and 10041206) and Bronco-DM tablets (HK-39022) (Batch no: 10031506), manufactured from one of its production lines following a complaint about a metal wire found in one tablet of its product, Bronco-DM tablets.

Investigation showed that the piece of metal wire might have come from a sieve used during production. The manufacturer has immediately suspended all production to facilitate DH investigation. So far, no adverse report had been received.

Further investigation by the DH could not ascertain that other products manufactured from the same production line were not affected by the defect. As such, Universal was directed to recall all 20 products manufactured from this production line. A list of the products under recall could be found at website: http://www.dh.gov.hk/english/press/2010/Recall_List(20101015).rtf.

Universal had set up hotlines for public enquiries. Members of the public were advised to inspect the medicines at hand before taking them. They should consult healthcare professionals if in doubt.

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