Drug News
藥 物 情 報

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This is a monthly digest of local and overseas drug safety news and information released by the Drug Office of the Department of Health in the month as stated above. For the latest news and information, please refer to public announcements or the website of the Drug Office of the Department of Health (http://www.drugoffice.gov.hk).

Safety Update

US, Australia: Concomitant use of protease inhibitors for HIV or hepatitis C and certain statin drugs can increase the risk of muscle injury

On 1 March 2012, the US Food and Drug Administration (FDA) updated the recommendations about the interactions between protease inhibitors for human immunodeficiency virus (HIV) or hepatitis C virus (HCV) and certain statin drugs. The concomitant use of both drugs might increase the risk of muscle injury (myopathy/ rhabdomyolysis). In the US, the labels for both the HIV protease inhibitors and the affected statins had been updated to contain consistent information about the interactions and dosage recommendations for those statins that might safely be co-administered with HIV or HCV protease inhibitors.

In response to the safety information of statin released by FDA, the Therapeutic Goods Administration (TGA) of Australia issued a safety alert on 1 March 2012 to announce that the agency would review the evidence associated with the use of statins and protease inhibitors.

In Hong Kong, there are around 241 and 21 registered pharmaceutical products which belong to the class of statins and protease inhibitors respectively. All are prescription medicines. Statins are indicated for hypercholesterolemia, whereas protease inhibitors have antiviral activity and are used in the treatment of HIV and HCV infections. A letter to healthcare professionals was issued on 2 March 2012. The matter will be 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.

Canada, Singapore: Serious abnormal heart rhythms and sudden death (cardiac arrest) are associated with the use of Domperidone Maleate

On 2 March 2012, Health Canada advised healthcare professionals to initiate domperidone at the lowest possible dose in adults to reduce the risk of serious ventricular arrhythmias (SVA) or sudden cardiac death (SCD). The Product Monographs for all domperidone products in Canada would be updated to include information about this risk, the new dosage and usage recommendations. The update was based on the recent epidemiological studies which showed that the use of domperidone might be associated with an increased risk of SVA or SCD, especially in patients taking daily doses greater than 30 mg, and in patients older than 60 years of age. Healthcare professionals were reminded to be cautious when prescribing domperidone to patients who were also taking drugs that prolonged the QT interval, had prolonged cardiac conduction intervals, particularly QTc, had significant electrolyte disturbances or underlying cardiac disease such as congestive heart failure.

On 20 April 2012, Health Sciences Authority (HSA) of Singapore had also issued a similar safety alert. The package inserts of domperidone products in Singapore were being updated to include the associated risk of SVA and SCD.

In Hong Kong, there are around 53 registered pharmaceutical products containing the anti-emetic drug domperidone. The issue had been discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board on 28 February 2012. The Committee decided that the sales pack label

and/or package insert of the products containing domperidone should include safety information regarding the risk of cardiac disorder. In view of Health Canada's recommendation, a letter to healthcare professionals was issued on 8 March 2012.

Product complaints for Invega Sustenna Injections (Paliperidone palmitate)

The Department of Health (DH) was informed by Johnson & Johnson (HK) Ltd. (Johnson & Johnson) on 7 March 2012 about product complaints of possible cracks in the plastic syringe needle hub of the products, Invega Sustenna Injections 25mg, 50mg, 75mg, 100mg and 150mg.

According to Johnson & Johnson, the crack defects could be produced under stress conditions such as improper alignment of syringe and needle or use of excessive torque during needle assembly. Theoretically, cracks at the needle hub could cause leakage of the injection suspension and potentially result in a reduced efficacy if a lower than intended therapeutic dose was given, or an overdose if an additional dose was administered. The company identified 74 cases worldwide of cracks or leaks at the needle hub but none was found in Hong Kong. These 74 cases of cracks or leaks led to 1 possible case of reduced efficacy and 1 case of accidental eye exposure in a healthcare professional. Both were not related to any specific lot number of finished product or component.

In Hong Kong, Invega Sustenna Prolonged Release Suspension for IM Injection 25mg (HK-60143), 50mg (HK-60141), 75mg (HK-60145), 100mg (HK -60142) and 150mg (HK-60144) are registered by Johnson & Johnson. They are prescription medicines and are indicated for the acute and maintenance treatment of schizophrenia in adults. In light of above safety information, a letter to healthcare professionals was issued on 7 March 2012. DH would closely monitor the development of the issue.

UK, Singapore: Label update of Onglyza® (saxagliptin) on the associated risk of serious hypersensitivity reactions and acute pancreatitis

On 8 March 2012, Bristol-Myers Squibb, AstraZeneca and the Medicines and Healthcare products Regulatory Agency (MHRA) updated healthcare professionals of the new safety information to be included in the product information for Onglyza (saxagliptin). The update was based on a review of pharmacovigilance data including post-marketing reports which identified cases of serious hypersensitivity reactions and acute pancreatitis with the use of saxagliptin. The following recommendations had been made accordingly:

- Saxagliptin was contra-indicated in patients with a history of serious hypersensitivity reactions, including anaphylactic reaction, anaphylactic shock, or angioedema, to saxagliptin or any dipeptidyl peptidase 4 (DPP-4) inhibitor;
- Patients should be informed of the characteristic symptoms of acute pancreatitis such as persistent and severe abdominal pain.
- If serious hypersensitivity reactions or pancreatitis to saxagliptin were suspected, the treatment should be discontinued.

In Singapore, the package insert for Onglyza® has also been updated in March 2012 to include the above safety information.

In Hong Kong, Onglyza Tab 5mg (HK-59907) and 2.5mg (HK-60783) are registered by Bristol-Myers Squibb Pharma (HK) Ltd. and are prescription medicines. It is indicated for diabetic mellitus. A letter to healthcare professionals was issued on 8 March 2012 and the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

Australia, Singapore: Contamination of CSL Human Albumin (4% and 20%) with ethylene glycol

In March 2012, CSL Biotherapies (CSL) notified the TGA that some batches of human albumin solutions manufactured prior to 25 January 2012 had been contaminated with ethylene glycol because of an equipment failure. In response, TGA quarantined all batches of albumin as a precautionary measure for thorough safety assessment. Each affected batch would be tested by CSL to detect ethylene glycol according to the standard and sensitivity (to detect ethylene glycol at or above 0.5 parts per million (ppm), which was well below the internationally accepted safety limit for this compound) agreed by

TGA. Batches which could not detect harmful levels of ethylene glycol would then be released from quarantine. The ethylene glycol testing of all affected batches was completed by CSL in April. Out of the 96 batches of the quarantined human albumin investigated, the following results were noted:

- No ethylene glycol was detected in 78 batches and they were subsequently released from quarantine.
- 18 batches were found to contain low levels of ethylene glycol, and only one batch of Albumex 4 (3450700309), which had been quarantined in Australian hospitals and at the Australian Red Cross Blood Service, was recalled due to the presence of ethylene glycol at a concentration of $\geq$ 0.5 mg/L.

TGA conducted an audit on the manufacturing process at CSL and concluded that a crack in a heating/cooling jacket surrounding a storage tank for albumin solution was the cause of contamination. TGA had verified that the problem had been rectified and no problematic batches were detected after the repair. In this connection, TGA agreed that batches of albumin solution manufactured after 25 January 2012 needed not be quarantined.

CSL also informed TGA that a very small amount of albumin at low concentration was being used as a stabilising agent in CSL Biostate (plasma derived Factor VIII concentrate). Based on the theoretical maximum doses of Biostate and the highest level of ethylene glycol found in the Albumin, it was concluded that the potential amount of ethylene glycol being administered was many times below the maximum exposure as recommended in the European Medicines Agency (EMA) / International Committee for Harmonisation (ICH) guideline. Therefore, TGA advised that Biostate was not subject to the present recall actions.

Upon receiving the notification from CSL about this safety issue, the HSA of Singapore suspended the supply and use of all batches of CSL albumin products in public hospitals. Samples were tested in HSA's laboratory and one batch of Albumex 20® was found to contain ethylene glycol at a low level which was unlikely to pose a risk to patient safety. As a precautionary measure, HSA initiated a recall of all Albumex 20® manufactured by CSL in Australia.

In Hong Kong, Albumex 5 Infusion 12.5g/250ml (HK-58570) and Albumex 20 Infusion 10g/50ml (HK-58571) are registered by HK Red Cross Blood Transfusion Service (BTS), and are prescription medicines. DH was informed by BTS on 8 March 2012 regarding the news. Subsequently a total recall of the above products was initiated in Hong Kong and a press release was issued on the same day. The details of the recall was reported in this issue under the section of "Drug Recall".

Biostate Human Factor VIII for Inj 250IU (HK-50870) is registered by BTS, Aleviate for Inj 500IU (HK-53466) and 250IU (HK-53467) are registered by CSL Biotherapies Asia Pacific Ltd. and all are prescription medicines. All are manufactured by CSL in Australia. According to the certificate holder of Aleviate for Inj 500IU, the product had never been imported into Hong Kong. After preliminary assessment, the risk of offering treatment with these products was likely to be negligible. In addition, samples of the products had been taken for analysis and no ethylene glycol was detected in these products.

Canada: Health Canada endorsed important safety information on fluoroquinolone antibiotics

Following a public announcement about the risk of exacerbating muscle weakness in patients with myasthenia gravis after taking fluoroquinolone antibiotics in November 2011, Health Canada informed the healthcare professionals about the progress of the label updates on 9 March 2012. The labeling for all the innovator fluoroquinolone products had been updated to reflect the above safety information by January 2012, whereas the monographs for the generic products were being updated. The association between the exacerbation of myasthenia gravis and fluoroquinolone use had been established based on the review of post-marketing reports, which identified cases of serious adverse events, including deaths and the requirement for ventilatory support. As mentioned in Drug News No. 25, the risk appeared to occur only for oral or intravenous formulation.

In Hong Kong, there are about 182 registered pharmaceutical products containing

fluoroquinolones in oral or intravenous dosage forms. All are prescription medicines indicated for the treatment of adults with various bacterial infections such as infections of the respiratory tract, skin and urinary tract. A letter to healthcare professionals was issued on 8 November 2011 and the matter had been discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board on 28 February 2012. The Committee decided that the sales packs or package inserts of fluoroquinolones in oral or intravenous forms should be updated to include safety information in relation to the risk of fluoroquinolones-associated myasthenia gravis exacerbation.

UK: Batch recall of Cisplatin 1mg/ml, concentrate for solution for infusion

On 13 March 2012, Teva UK Ltd. recalled a batch (batch no. 09J29QG) of Cisplatin 1mg/ml, concentrate for solution for infusion 1 x 10ml because it had been given a three year shelf-life whereas the approved shelf-life was 18 months. Whilst the available stability data did not support a three year shelf-life, retained samples from this batch had recently been tested and were found to comply with the required specifications. Remaining stocks of this batch would be quarantined and returned to the original supplier.

In Hong Kong, the above anti-neoplastic product is registered under the name Platosin Inj 1mg/ml (HK-39197) by the International Medical Co. Ltd. and is a prescription medicine. According to the company, the batch currently supplied in Hong Kong is of 18 months' shelf-life and the above batch had not been imported into Hong Kong.

EU: Withdrawal of applications for an extension of the indication for Exelon and Prometax (rivastigmine) Patches by Novartis Europharm Ltd.

On 15 March 2012, the European Medicines Agency (EMA) alerted the public that Novartis Europharm Ltd. (Novartis) had decided to withdraw its applications for including a new indication of two medicines containing rivastigmine, Exelon and Prometax, 4.6 mg/24h and 9.5 mg/24h transdermal patches. The application was submitted in March 2011 to extend the marketing authorisations of these products to include an indication for the symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease. According to Novartis, the decision was made as the company could not provide additional data within the timeframe as requested by the Agency's Committee for Medicinal Products for Human Use (CHMP). In the EU, both medicines continued to be authorised in the currently approved indication, which was for the treatment of mild to moderately severe Alzheimer's dementia.

In Hong Kong, there are two registered prescription medicines containing rivastigmine, Exelon Patch 5 (4.6mg/24h) (HK-56982) and Exelon Patch 10 (9.5mg/24h) (HK-56983), are registered by Novartis Pharmaceutical (HK) Ltd. The local approved indication of Exelon Patches are for the treatment of mild to moderate dementia of the Alzheimer's type and dementia associated with Parkinson's disease which are adopted from the US FDA. In view of EMA's recommendation, a letter to healthcare professionals was issued on 16 March 2012 and the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

UK: The risk of potential leaks with 5L Physioneal clear-flex bags

On 15 March 2012, MHRA alerted healthcare professionals of a recent increase in complaints of leaks associated with products of a peritoneal dialysis (PD) solution, the 5L Physioneal Clear-Flex products. The leaks were due to a tear in the Clear-Flex bag when the patient was activating the peel seals during preparation prior to the start of automated PD (APD). The leak might affect product sterility but no relevant adverse events (e.g. peritonitis) related to the product were reported so far. The frequency of leaking bags was also found to be very low. Healthcare professionals were reminded to check the 5L Physioneal Clear-Flex bags for leaks and follow the instructions provided in the product training materials. They were advised to alert their patients of this recommendation.

In Hong Kong, five pharmaceutical products are registered under the brand Physioneal, namely, Physioneal 40 Dextrose 2.5% PD Solution (HK-53650), Physioneal 40 Dextrose 1.5% PD Solution (HK-53651), Physioneal 40 Dextrose 4.25% PD Solution (Singapore) (HK-57073), Physioneal 40 Dextrose 2.5% PD Solution (Singapore) (HK-

57074) and Physioneal 40 Dextrose 1.5% PD Solution (Singapore) (HK-57075). They are registered by Baxter Healthcare Ltd. According to the company, the products registered in Hong Kong were not packed in Clear-Flex bags. Nevertheless, a letter to healthcare professionals was issued on 2 April 2012 to remind them and advise their patients of the importance of checking the bags for leaks and proper use and handling of the products.

EU: Positive benefit-risk balance of Protelos/ Osseor (strontium ranelate) remained with new contraindications and revised warnings

Further to the safety issue as reported in Issue No. 23 and 25 of Drug News, CHMP issued a public announcement on 16 March 2012 that it had finalised a review of Protelos and Osseor (strontium ranelate). CHMP concluded that these products were effective for treatment of postmenopausal women with osteoporosis but the product information should be updated to better address the associated risk of venous thromboembolism (VTE) and severe skin reactions. Their uses were contraindicated in patients with a history of VTE, temporarily or permanently immobilised patients and re-evaluation for the need of continued treatment by doctors was advised in patients over 80 years of age at risk of VTE because these 3 groups were found to have higher risks of VTE. In addition, the product information should include the signs and symptoms of severe skin reactions, such as drug rash with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), as well as their time-to-onset because the best management of these reactions depended on early diagnosis and prompt cessation of treatment. Healthcare professionals and patients were reminded of the risks and stopping treatment immediately and permanently if symptoms of severe skin reactions developed.

In Hong Kong, Protos Granules for Oral Suspension 2g, (HK-53835) is registered by Servier Hong Kong Ltd., and is a prescription medicine used for treatment of osteoporosis in postmenopausal women to reduce the risk of fracture at spine and hips. A letter to healthcare professionals was issued on 19 March 2012 and the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

Canada: Label update of Pradax® (dabigatran etexilate) regarding kidney function assessment and use in patients with certain heart valve diseases or artificial heart valves

Further to the safety issues as reported in Issues No. 24 and 25 of Drug News, Boehringer Ingelheim (Canada) Ltd. informed healthcare professionals on 16 March 2012 that the Product Monograph for Pradax® (dabigatran etexilate) in Canada was updated to include the following two new recommendations.

- As renal impairment was a risk factor for bleeding with Pradax®, renal function assessment should be done before starting treatment to rule out severe renal impairment (i.e. CrCl < 30 mL/min) and during the treatment if renal function deterioration was suspected such as hypovolemia, dehydration, and with certain co-medications. In patients older than 75 years of age or with moderate renal impairment, renal function should be assessed at least once a year.
- Pradax® was not recommended in patients with hemodynamically significant rheumatic valvular heart disease or in patients with prosthetic heart valves because its safety and efficacy had not been studied in these groups.

Healthcare professionals were reminded not to prescribe Pradax® in patients with severe renal impairment or at high risk of bleeding. They were advised to monitor for signs of bleeding and stop Pradax® when severe bleeding occurred.

In Hong Kong, Pradaxa (dabigatran) is an anticoagulant registered as 75mg, 110mg and 150mg capsules by Boehringer Ingelheim (HK) Ltd. and is a prescription medicine. Letters to healthcare professionals were issued on 19 August 2011 and 4 November 2011. The matter was discussed at the meeting of the Registration Committee of the Pharmacy and Poisons Board on 26 April 2012. The Committee decided that the sales pack label and/or package insert for all strengths of the products should include safety information regarding the need for renal function assessment and contraindications for use in patients with severe renal impairment . The label update regarding the use in patients with certain heart valve diseases or

artificial heart valves will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

Canada: Increased risk of high-grade prostate cancer with the use of Finasteride (Proscar, Propecia) and dutasteride (Avodart, Jalyn)

Further to the previous announcement made by the FDA as reported in Issue No. 20 of Drug News, Health Canada informed the public that finasteride and dutasteride might be associated with an increased risk of high-grade prostate cancer on 19 March 2012. The information was based on the review of two clinical trials, namely the Prostate Cancer Prevention Trial (PCPT) and the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial. Both trials showed that chronic daily use (over 4 years) of finasteride (5 mg) and dutasteride in men aged 50 years and older was associated with a small but statistically significant increased risk of high-grade prostate cancer. The Canadian labels for the brand name drugs had been updated to include this risk and to emphasize that these drugs were not approved for the prevention of prostate cancer. Healthcare professionals were advised to rule out other urological diseases, including prostate cancer, before prescribing these drugs.

In Hong Kong, there are 21 finasteride and 2 dutasteride-containing pharmaceutical products registered respectively. All are prescription medicines. Both drugs are indicated for the treatment of symptomatic benign prostatic hyperplasia, and finasteride is also used for the treatment of men with male pattern hair loss. A letter to healthcare professionals was issued on 10 June 2011. The matter was discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board on 6 September 2011. The Committee decided that the sales pack label and/ or package insert of products containing the concerned ingredients should indicate that their uses might increase the risk of high-grade prostate cancer, and these products were not approved for the prevention of prostate cancer.

Canada: Lot recall of Apo-Ramipril 5mg

On 19 March 2012, Health Canada announced that Apotex Inc. voluntarily recalled a lot (Lot number: JR2178) of Apo-Ramipril 5mg Capsules because this lot had been found to contain intact but empty capsules. This implied that patients taking them might not receive the dose of medication needed to treat their medical condition. In addition, it would be difficult to determine whether the capsule of Apo -Ramipril 5 mg was empty because it was not transparent. Hypertension without proper treatment might lead to heart attack, stroke, kidney problems, internal bleeding and improper blood circulation. Patients were advised to consult their healthcare professionals if they had used this product and were concerned about their health.

In Hong Kong, Apo-Ramipril Cap 5mg (HK-57336) is registered by Hind Wing Co Ltd. and is a prescription medicine. It is used for the treatment of hypertension and congestive heart failure. According to the company, the above batch had not been imported into Hong Kong.

Suspension of the use of specific batches of Prevenar 13 vaccine and Rotateq oral vaccine in Portugal

On 23 March 2012, DH was informed by Pfizer Corporation HK Ltd. (Pfizer) that the Portuguese National Authority of Medicines and Health Products, I.P. (INFARMED) had suspended on a national basis the use of one batch of Prevenar 13 vaccine (Lot F73745) and one batch of Rotateq oral vaccine (Lot 1590AA) on a national basis as a precautionary measure. According to Pfizer, the company was informed by the INFARMED of a fatality involving a 5-month-old child who was reported to have respiratory arrest following concomitant vaccination with the two vaccines. As a precautionary measure, INFARMED had suspended the use of the 2 batches of the vaccines involved until evaluation of the present situation was concluded.

In Hong Kong, Prevenar 13 vaccine (HK-59600) is registered by Pfizer and Rotateq oral vaccine (HK-55037) is registered by Merck Sharp & Dohme (Asia) Limited (MSD). Both are prescription medicines. Prevenar 13 vaccine is a 13 valent pneumococcal conjugate vaccine against invasive disease, pneumonia & acute otitis media caused by *Strep pneumoniae*. Rotateq oral vaccine is a rotavirus vaccine used for the prevention of rotavirus gastroenteritis. According to Pfizer, the suspended lot of Prevenar 13 vaccine (Lot F73745)

was derived from bulk lot 917690, and none of these lots had been imported into Hong Kong. As confirmed with MSD, the suspended lot of Rotateq oral vaccine (Lot 1590AA) and its sister lots had not been imported into Hong Kong.

UK: The risks of too rapid increases in serum sodium with tolvaptan (Samsca) and the need for close monitoring and avoidance of concomitant use of other drugs that increased serum sodium

On 26 March 2012, Otsuka Pharmaceutical Europe Ltd. and the MHRA alerted healthcare professionals about the risks of too rapid increases in serum sodium when using tolvaptan. Although tolvaptan was used in treating hyponatraemia, correcting serum sodium faster than the suggested rate was known to cause osmotic demyelination and have neurological sequelae. The following measures were recommended to minimize this risk:

- Close monitoring of serum sodium during tolvaptan treatment was recommended, especially in patients with very low baseline serum sodium (<120 mmol/L) or in those at high risk of demyelination syndromes.
- Close monitoring of serum sodium and administration of hypotonic fluid were recommended for patients with too rapid sodium correction exceeding 6 mmol/L during the first 6 hours of administration or 8 mmol/L during the first 6-12 hours.
- Discontinuation of tolvaptan and followed by administration of hypotonic fluid were recommended for sodium correction exceeding 12 mmol/L in 24 hours or 18 mmol/L in 48 hours.
- Co-administration of tolvaptan with other treatments for hyponatraemia, or medications that increased serum sodium concentration or with a high sodium content, was not recommended.

The product information for tolvaptan (Samsca) had been updated accordingly.

In Hong Kong, Samsca Tab 15mg (HK-59910) and 30mg (HK-59911) are registered by Otsuka Pharmaceutical Co Ltd. and are prescription medicines. They are used for the treatment of euvolaemic and hypervolaemic hyponatraemia including in heart failure, syndrome of inappropriate antidiuretic hormone secretion, and cirrhosis. A letter to healthcare professionals was issued on 2 April 2012 and the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

US: Revised recommendations against the potential risk of abnormal heart rhythms with the use of Celexa (citalopram hydrobromide)

As reported in Issue No. 23 of Drug News in August 2011, FDA announced that the daily dose of Celexa (citalopram hydrobromide) should not be greater than 40 mg because it could cause abnormal changes in the electrical activity of the heart. On 28 March 2012, FDA clarified the dosing and warning recommendations for citalopram. The use of citalopram was discouraged in patients with certain conditions because of the risk of QT prolongation. However, as its use might be important for some of those patients, the drug label had been changed to describe the particular caution that needed to be taken when citalopram was used in such patients. The labeling recommendation for patients with congenital long QT syndrome had been changed from "contraindicated" to "not recommended" because some of these patients without other viable alternatives might benefit from a low dose of citalopram. ECG monitoring and/ or electrolyte monitoring were recommended if citalopram had to be used in patients having risk of QT prolongation. In addition, citalopram should be discontinued in patients with persistent QTc measurements greater than 500ms.

In Hong Kong, a total of 19 citalopram-containing products are registered and are prescription medicines. They are indicated for the treatment of depression. A letter to healthcare professionals was issued on 25 August 2011. The matter had been discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board on 6 September 2011. The Committee decided that the maximum daily dosage of citalopram should be limited to 40mg and the sales pack label and/or package insert of citalopram-containing products should be updated to include information regarding the abnormal heart rhythm associated with high doses of citalopram. DH will keep vigilant against any updated safety news of the drug from other regulatory authorities.

Total recall of Ospexin Cap 500mg (HK-33816) and Ospexin Cap 250mg (HK-33817)

On 7 March 2012, DH endorsed the voluntary recall of all batches of Ospexin Cap 500mg (HK-33816) and Ospexin Cap 250mg (HK-33817) from consumers by a licensed drug wholesaler, Novartis Pharmaceuticals (HK) Ltd (Novartis), on quality grounds. The products contain cephalexin and are antibiotics for bacterial infections. They can only be sold on prescription and under the supervision of pharmacists at registered pharmacies.

The recall was initiated because the products' Austrian manufacturer, Sandoz GmbH, found that both products had failed several tests during an ongoing stability study. According to Novartis, the tests on dissolution, water content and capsule shell colour of the products stored at 30°C and a relative humidity of 75% for 12 months were found to be unsatisfactory. Preliminary investigation revealed that the problem could be due to the ineffectiveness of the packing materials in protecting the products from moisture under the above storage conditions.

The two products had been supplied to Hospital Authority (HA), private hospitals, DH clinics, private doctors and pharmacies. Ospexin Cap 500mg had also been exported to Macau. DH had alerted HA, private hospitals, professional healthcare bodies and the Macau authority about the matter and closely monitored the recall. DH had not received any adverse event reports of the products concerned and a press statement was released on the same day to alert the public of the recall.

Total recall of Albumex 5 (HK-58570) and Albumex 20 Infusion (HK-58571)

On 8 March 2012, DH instructed a licensed drug wholesaler, Hong Kong Red Cross Blood Transfusion Service (HK Red Cross), to recall all Albumex 5 Infusion 12.5g/250ml (HK-58570) and Albumex 20 Infusion 10g/50ml (HK-58571), on quality grounds. The products contain human albumin and are used for shock or in plasma exchange. They can only be sold on prescription and under the supervision of pharmacists at registered pharmacies.

DH received notification from the HK Red Cross that the product manufacturer in Australia, CSL Limited, had found some of the Albumex products being contaminated with ethylene glycol. The event came to light after a follow up investigation of a small leak of ethylene glycol (in late January 2012) in a pasteurisation vessel used in the manufacture of the products. Ethylene glycol is a substance used to control temperature during the manufacturing process. Toxic effects of ethylene glycol include central nervous system effects similar to ethanol, anion gap metabolic acidosis, and acute renal failure. Toxicity due to ethylene glycol occurs acutely and delayed effects beyond 72 hours will not be expected.

The products had been supplied to HA and private hospitals. DH had alerted HA and private hospitals about the matter and closely monitored the recall. DH had not received any adverse event reports of the said products and a press statement was released on the same day to alert the public of the recall.

Samples of the available stocks of Albumex 5 and Albumex 20 (two batches each) were taken for analysis. The laboratory test finding revealed the presence of ethylene glycol in only one batch of Albumex 20 (Batch number: 3470500441). Furthermore, TGA also confirmed that other batches in Hong Kong were not affected. Thus, the unaffected batches were put back into the market.

Batch recall of B Braun Sodium Bicarbonate 8.4% Infusion (HK-28230)

On 26 March 2012, DH instructed a licensed drug wholesaler, B Braun Medical (HK) Limited (B Braun), to recall from shelf one batch (Batch number: 111358021) of its Sodium Bicarbonate 8.4% Infusion (HK-28230) as part of a global act due to suspected quality defect. Sodium Bicarbonate 8.4% Infusion is an intravenous solution primarily indicated for metabolic acidosis and urine alkalisation.

Through its surveillance scheme, DH learnt that the UK MHRA had initiated a recall of one batch of the above product subsequent to a global recall by the product's manufacturer in Germany, B Braun Medical Melsungen. According to the manufacturer's in-house finding, precipitation was detected in some items and was likely to be aluminium salt. The precipitation tended to flocculate in aggregates of different sizes and could cause or contribute to the development and worsening of adverse effects such as embolism.

Drug Recall

B Braun imported one of the recalled batch into Hong Kong in 2011 and had supplied to HA, private hospitals, public and private clinics, and also exported to Macau. DH had alerted HA, private hospitals, professional healthcare bodies and the Macau authority about the matter and closely monitored the recall. DH had not received any adverse event reports of the product concerned and a press statement was released on the same day to alert the public of the recall.

Total recall of Carboplatin 10mg/ml Injection (Ebewe) (HK-43913)

On 29 March 2012, DH endorsed the recall by Novartis Pharmaceutical (HK), a licensed drug wholesaler, of all batches of its Carboplatin 10mg/ml Injection (Ebewe) (HK-43913) from shelves as part of an international effort to curb quality failure in the product. It is indicated for the treatment of various cancers. It can only be sold on prescription and under the supervision of pharmacists at registered pharmacies.

The recall was initiated after the product's Austrian manufacturer, Ebewe Pharma, recalled the product concerned as a precautionary measure because precipitates were identified in several batches of samples retained routinely as part of good manufacturing practice. The precipitates were likely from either the active drug ingredient or its degradation. Further, preliminary assessment indicated that the precipitates were probably the result of stability issues. The concern was that the precipitates in injectable products might pose risks including granulomas or even vascular occlusions.

The product came in 15ml and 45ml vials which were supplied to HA, private hospitals, private doctors, and also exported to Macau. DH had alerted HA, private hospitals, professional healthcare bodies and the Macau authority about the matter and closely monitored the recall. DH had not received any adverse event reports of the said products and a press statement was released on the same day to alert the public of the recall.

Members of the public were advised to consult their healthcare providers if they were in doubt or felt unwell after using the above products.

Selling any drug not of the nature, substance or quality demanded by the purchaser is an offence under Section 52(1) of the Public Health and Municipal Services Ordinance (Cap 132). The maximum penalty involved is $10,000 and three months' imprisonment.

Drug Incident

Warning on a slimming product found with undeclared and banned drug ingredients

On 6 March 2012, DH issued a press statement to appeal to members of the public not to buy or consume a slimming product called "The Extreme-thin Fat Burning Bomb"「極瘦脂肪燃燒彈」 as it was found to undeclared and banned drug ingredient that was dangerous to health.

DH was notified by the HA about a 52-year-old lady who was hospitalized because of dizziness and palpitation, after consumption of the above slimming product. The laboratory test finding showed the presence of the banned Western medicine sibutramine in the product. The product was not purchased from a local source.

Sibutramine is a Part I poison and was once a Western medicine used as an appetite suppressant. Since November 2010, products containing sibutramine have been banned because of increased cardiovascular risk.

Weight control should only be achieved through a good diet and appropriate exercise. People ought to consult healthcare providers for professional advice if they have questions and definitely before using any medication for weight control.

Man arrested for allegedly selling unregistered pharmaceutical product

On 30 March 2012, a joint operation was conducted by DH and the Police resulting in the arrest of a 53-year-old man for suspected illegal sale of two boxes of cold and flu medicine 「パブロン S 錠」 manufactured by Taisho Pharmaceutical Co., Ltd., which was unregistered pharmaceutical product.

Drug Incident

The product「パブロン S 錠」was found to be sold on the Internet auction website during DH's surveillance programme. Laboratory test findings revealed that the product contained paracetamol.

Paracetamol is a western medicine and is used for the management of pain and fever. Although the side effects are usually mild, taking high dose may result in liver damage.

A press statement related to the case was issued on the same day.

DH appealed to members of the public not to buy or consume unknown or doubtful products from the market or the Internet as they may contain undeclared and banned drug ingredients that are dangerous to health.

A product containing any western drug ingredient must be registered under the Ordinance before it can be sold in Hong Kong. The products mentioned in the above incidents were not registered pharmaceutical products under the Pharmacy and Poisons 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. Members of the public should stop using the aforementioned products immediately if they had them in their possession. They were also advised to consult healthcare professionals if they felt unwell or were in doubt after taking the products. They should destroy, dispose or submit them to the Department's Drug Office during office hours.

Useful Contact

Drug Complaint:

Tel: 2572 2068

Fax: 2147 0457 & 2123 1996

E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920

Fax: 2147 0457

E-mail: adr@dh.gov.hk

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

Post: ***Pharmacovigilance Unit,***
Drug Office, Department of Health,
3/F, Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon

The purpose of Drug News is to provide healthcare professionals with a summary of local and overseas drug safety news released. Healthcare professionals are advised to keep update with the information and provide corresponding advice or therapeutic measure to patients and public.