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

The Mainland: Injectable ambroxol hydrochloride may be associated with severe hypersensitivity reactions

On 3 September 2012, the State Food and Drug Administration (SFDA) of the Mainland alerted healthcare professionals and the traders on the risk of severe hypersensitivity reactions associated with injectable ambroxol hydrochloride. In the year of 2011, the National Centre for Adverse Drugs Reaction (ADR) Monitoring of China received 2,973 cases of ADRs related to injectable ambroxol hydrochloride. Among these, 169 were severe cases and the main presenting clinical features included hypersensitivity reactions, dyspnoea and anaphylactic shock. Out of the 169 severe cases, 79 was related to paediatric patients with 51 cases of ambroxol overdose. Healthcare professionals were reminded to pay particular attention to the dosage regime of ambroxol injection including the dose adjustment in individual patients and avoid unapproved indications when prescribing ambroxol injection. In addition, ambroxol injection should be used in caution in patients with history of hypersensitivity and allergy such as bronchial asthmatics. Besides, ambroxol injection should not be co-administered with any medicines and the concomitant use with alkaline liquids, cephalosporins or Chinese medicines should be avoided. The pharmaceutical manufacturers were advised to revise the product inserts accordingly to highlight the risk of severe allergic reactions.

In Hong Kong, two injectable ambroxol products, namely Nadoxol Inj 15mg/2ml (HK-50296) and Huons Ambroxol HCl Inj 15mg/2ml (HK-57625), are registered. They are registered by Healthcare Pharmascience Ltd. and Julius Chen & Co. (HK) Ltd. respectively. Ambroxol is a mucolytic indicated for the treatment of respiratory diseases caused by respiratory mucosa-secretion disturbance. The product inserts of the above products had included the warning on the risk of severe hypersensitivity reactions. Drug Office had not received any relevant adverse event report in connection with the use of injectable ambroxol but will keep vigilant against any updated safety issue of the product. In view of SFDA's recommendations, a letter to healthcare professionals was issued on 4 September 2012.

UK: Simplification of the use of intravenous acetylcysteine for paracetamol overdose

On 3 September 2012, the Medicines and Healthcare products Regulatory Agency (MHRA) of the UK announced the recommendations of the Commission on Human Medicines (CHM) regarding the use of intravenous (IV) acetylcysteine for the treatment of acute paracetamol overdose. IV acetylcysteine (given within 8 hours) was almost 100% effective in preventing severe liver damage and death caused by paracetamol overdose. There had been a number of reports of deaths and liver damage from paracetamol overdose in patients who presented within 8 to 10 hours but were not treated because they were not thought to be at risk. Therefore, the review by CHM was conducted. In order to simplify treatment decisions CHM recommended that:

a. IV acetylcysteine should be indicated in patients with paracetamol overdose:

- who had taken a staggered overdose (where staggered was defined as ingestion of

paracetamol over a period of 1 hour or more) irrespective of the plasma paracetamol level;

- in whom there was doubt over the time of paracetamol ingestion irrespective of the plasma paracetamol level; or
- who presented with a timed plasma paracetamol level on or above a single treatment line joining points of 100mg/L at 4 hours and 15mg/L at 15 hours nomogram, regardless of risk factors of hepatotoxicity. For details of the nomogram, please visit MHRA's website at http://www.mhra.gov.uk/home/groups/pl-p/documents/drugsafetymessage/con184396.pdf;

b. an increase in the duration of administration of the first dose of IV acetylcysteine from 15 minutes to 1 hour;

c. removal of hypersensitivity as a contraindication to treatment with acetylcysteine;

d. the provision of weight-based dosing tables for adults and children; and

e. the provision of a Technical Information Leaflet to reduce the risk of administration errors.

In Hong Kong, three injectable acetylcysteine products are registered: Fluimucil Inj 300mg/3ml (HK-42254), Hidonac Solution for Infusion 200mg/ml (HK-48124) and DBL Acetylcysteine Inj Concentrate 2g/10ml (HK-57409), which are indicated for the treatment of paracetamol poisoning. The first two products are registered by Zenfields (HK) Ltd., whereas the third product is registered by Hospira Ltd. In view of MHRA's recommendations, a letter to healthcare professionals was issued on 4 September 2012, and 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 (Registration Committee) of the Pharmacy and Poisons Board.

Canada: Risk of myelosuppression, pulmonary toxicity, renal and hepatic toxicity as a result of overfilled vials of BiCNU® (carmustine for injection, USP) 100 mg/vial

On 4 September 2012, Heath Canada announced that Bristol-Myers Squibb (BMS) Canada recalled four batches of the BiCNU® (carmustine for injection USP) 100mg/vial (lot numbers: 9H4208A, 9H4210A, 0B7003A and 1C7005A). This recall was conducted as a precautionary measure due to the discovery of an overfilled vial of carmustine during routine stability testing. Subsequent investigation had reviewed that the occurrence of overfilled vial was very low. However, this identified defect could result in patients receiving a dose greater than prescribed and patients could be at risks, including myelosuppression, susceptibility to serious infections, bleeding, pulmonary toxicity and renal toxicity as well as other serious adverse effects such as hepatic toxicity. Healthcare professionals should be alerted on these symptoms in patients received BiCNU®.

In Hong Kong, BiCNU for Inj 100mg (HK-05144) is registered by BMS Pharma (HK) Ltd. It is a prescription medicine indicated for the treatment of cancer such as multiple myeloma and brain tumours. BMS confirmed that the affected batches had not been imported into HK.

UK: Batch recall of Cymevene 500mg Powder for Infusion (ganciclovir sodium)

On 5 September 2012, MHRA announced that Roche Products Ltd. recalled a batch of Cymevene 500mg Powder for Infusion (lot number: N0019) because a small number of reports of damaged vials were received resulting in the concerns of sterility assurance. The recalled product was manufactured by JHP Pharm. LLC in the US.

In Hong Kong, Cymevene for Inj 500mg (USA) (HK-60055) manufactured by JHP Pharm. LLC is registered by Roche HK Ltd. (Roche). It is a prescription medicine indicated for the prevention and treatment of life- or sight-threatening cytomegalovirus disease in immunocompromised individuals. According to Roche, the product had

not been imported and marketed in Hong Kong. Roche also confirmed that Cymevene for Inj 500mg (HK-32791) manufactured by F Hoffmaan-La Roche Ltd. in Switzerland which is marketed in Hong Kong was not affected by the incident.

US: Rare cases of serious burns with the use of over-the-counter topical muscle and joint pain relievers

On 13 September 2012, the Food and Drug Administration (FDA) of the US alerted the public that rare cases of serious skin injuries had been reported with certain over-the-counter (OTC) topical products. These OTC topical preparations were for the relief of mild muscle and joint pain, and were available as single- or combination-ingredient formulations that contained menthol, methyl salicylate, or capsaicin. Following their use, there had been rare cases of serious burns, some had severe complications requiring hospitalization. In many cases, the burns occurred after only one application resulting in severe burning or blistering occurring within 24 hours of the first application. Based on the reported cases, the majority of second- and third-degree burns occurred with the use of products containing menthol as the single active ingredient, and products containing both menthol and methyl salicylate, in concentrations greater than 3% menthol and greater than 10% methyl salicylate. Few cases reported using a capsaicin-containing product. Healthcare professionals were advised to counsel patients on how to use the products appropriately and inform them about the risk of serious harms, such as pain, swelling, or blistering of the skin, and advise patients to discontinue using the products once experienced such symptoms.

In Hong Kong, there are about 95 topical pharmaceutical products containing menthol and/or methyl salicylate registered for relieving muscle and joint pain. Nil registered pharmaceutical product containing capsaicin. So far, DH had not received any relevant adverse drug reaction report. In view of FDA's recommendations, a letter to inform healthcare professionals was issued on 14 September 2012. DH will keep vigilant against any updated safety news of the products.

US: Ongoing safety review of Parkinson's drug Mirapex (pramipexole) and possible risk of heart failure

On 19 September 2012, FDA informed the public about a possible increased risk of heart failure with Mirapex (pramipexole). FDA evaluated a pooled analysis of randomized clinical trials and found that heart failure was more frequent with Mirapex than with placebo; however, these results were not statistically significant. In addition, FDA evaluated two epidemiologic studies that suggested an increased risk of new onset of heart failure with Mirapex use. However, it was difficult to determine whether the increased risk of heart failure was related to Mirapex use or other influencing factors due to study limitations. FDA was continuing to work with the manufacturer to clarify the causality between heart failure and Mirapex, and would update the public once more information was available. Healthcare professionals were advised to follow the recommendations in the drug label when prescribing Mirapex and counsel patients to seek medical attention if they experienced symptoms of heart failure while taking Mirapex.

In Hong Kong, there are 8 registered pramipexole-containing pharmaceutical products. They are prescription medicines indicated for the treatment of idiopathic Parkinson's disease and for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome. In view of FDA's recommendations, a letter to healthcare professionals was issued on 20 September 2012. DH will keep vigilant against any updated safety news of the product.

US: Batch recall of Fibrin Sealant (Human) Evicel and Thrombin Topical (Human) Evithrom

On 26 September 2012, FDA announced that Ethicon, Inc. recalled several batches of Fibrin Sealant (Human) Evicel and Thrombin Topical (Human) Evithrom. It was due to a manufacturing process deviation that may have potentially led to the production of vials of thrombin with decreased potency. This manufacturing deviation may affect products that were produced before December 25, 2011 and this deviation was discovered through an internal review of the manufacturing process. FDA

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believed this potential decrease in potency did not pose a risk to patients as the thrombin level would still be effective in clot formation. However, customers were required to return the affected products with the lot numbers shown on the FDA website.

In Hong Kong, Evicel Solutions for Sealant 1ml (HK-61387), 2ml (HK-61386) and 5ml (HK-61369) are registered by Johnson & Johnson (HK) Ltd. (J&J). They are prescription medicines indicated as supportive treatment for improvement of haemostasis in surgery where standard surgical techniques are insufficient. J&J confirmed that the products had not been imported into Hong Kong. For "Evithrom", it is not a registered pharmaceutical product in Hong Kong.

Drug Recall

Batch recall of Irinotecan Concentrate for Infusion 100mg/5ml (HK-54038)

On 10 September 2012, DH endorsed a licensed drug wholesaler, Hospira Ltd. (Hospira), to recall from the market one batch of Irinotecan Concentrate for Infusion 100mg/5ml (lot number: Y073775AA), because of a quality issue. Irinotecan is an anti-cancer drug and is a prescription medicine which can only be sold with doctor's prescription and under the supervision of pharmacists at registered pharmacies.

The recall was initiated because the product's Australian manufacturer, Hospira Australia Pty. Ltd., had received four complaints in Europe, one related to batch Y073775A and three related to batch Y083775A. The complaints were related to breakage at the neck of the vial upon handling which might pose the risk of injury to health professionals and affect the sterility of the product. The root cause of breakage was excessive capping head pressure applied during the capping and crimping processes in the manufacture of these two batches. This was a global recall and only one of the affected batches had been imported into Hong Kong.

A total of 3,240 vials from the affected batch (lot number: Y073775AA (repacked from Y073775A)) were imported in December 2011 and all were supplied to the Hospital Authority. DH had alerted professional healthcare bodies about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction report. A press statement was released on the same day to alert the public of the recall.

Total recall of Typhim Vi (Typhoid Vaccine) (HK-36827)

On 14 September 2012, DH instructed a licensed drug wholesaler, Sanofi-Aventis HK Ltd. (Sanofi-Aventis), to conduct a total recall of Typhim Vi (Typhoid Vaccine) from the market because of a quality issue. Typhim Vi is indicated for the prevention of typhoid fever. It is a prescription medicine which can only be sold with doctor's prescription and under the supervision of pharmacists at registered pharmacies.

The recall was initiated because the product's French manufacturer, Sanofi Pasteur S.A., found out several failure test results regarding the antigen content during release testing, which might affect the efficacy of the vaccine. This issue was due to the heterogeneity at the end of the filling process of the finished product. Heterogeneity was caused by the formation of foam, which entrained the active component (polysaccharide) resulting in a decrease in the polysaccharide concentration of the final bulk product.

According to Sanofi-Aventis in Hong Kong, Typhim Vi had been supplied to DH clinics, private doctors, private hospitals, pharmacies, and exported to Macau. DH had alerted the relevant parties about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction report. A press statement was released on the same day to alert the public of the recall.

Drug Incident

Woman arrested for illegal sale of unregistered pharmaceutical product containing vitamins on the Internet

On 6 September 2012, a joint operation was conducted by DH and the Police resulting in the arrest of a 33-year-old woman for illegal sale of an unregistered pharmaceutical product that claimed to contain vitamins.

Through the DH's surveillance programme, the product "GNC Prenatal Formula with Iron 120 Caplets" was offered for sale in an Internet website. The product is a pharmaceutical product which is not registered with the Pharmacy and Poisons Board. The product label indicates it contains vitamins.

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

A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. Possession or sale of unregistered pharmaceutical products is an offence under the Pharmacy and Poisons Ordinance (Cap 138). The maximum penalty is a fine of $100,000 and two years' imprisonment.

A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. The product mentioned in the above incident was not registered pharmaceutical product under the Ordinance in Hong Kong. Its safety, quality and efficacy cannot be guaranteed. Members of the public were exhorted not to use products of unknown or doubtful composition. They should stop using the aforementioned product immediately if they had it in their possession and to consult healthcare professionals if they felt unwell after taking the product. The product should be destroyed, disposed or submitted 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.