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

EU / US / Canada: A new contraindication for Pradaxa (dabigatran etexilate) in patients with prosthetic heart valves

As reported in Issue No. 29 of Drug News, Health Canada alerted healthcare professionals that the Product Monogragh of Pradaxa (dabigatran etexilate) was updated. Pradaxa 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. On 21 December 2012, Health Canada announced that Pradaxa should not be used in patients with artificial heart valves (also known as prosthetic heart valves) due to the risk of strokes, bleeding, heart attacks, and blood clots forming on the artificial heart valves. This change was based on the interim results from a phase II trial (RE-ALIGN) which compared dabigatran etexilate and warfarin in a total of 252 patients with prosthetic heart valves. More thromboembolic events (mainly strokes and symptomatic/asymptomatic prosthetic valve thrombosis) and more bleeding events were observed with dabigatran etexilate than with warfarin, especially in patients who recently had mechanical valve replacement surgery. As a result, Boehringer Ingelheim decided to discontinue the study and update the worldwide labelling of Pradaxa to add a contraindication in patients with prosthetic heart valves.

On 13 December 2012, the Committee for Medicinal Products for human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending a variation to the terms of the marketing authorisation for Pradaxa to add a new contraindication as follows: “Prosthetic heart valves requiring anticoagulant treatment”.

On 19 December 2012, the Food and Drug Administration (FDA) of US also informed healthcare professionals and the public that Pradaxa should not be used to prevent stroke or blood clots (major thromboembolic events) in patients with mechanical prosthetic heart valves.

In Hong Kong, Pradaxa is an anticoagulant registered as 75mg capsules (HK-57316), 110mg capsules (HK-57315) and 150mg capsules (HK-60516) by Boehringer Ingelheim (HK) Ltd. and is a prescription medicine. Various safety alerts on Pradaxa had been released by several overseas regulatory authorities which had been reported in Issues No. 24, 25, 29 and 31 of Drug News. The issue related to renal function assessment had been 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 in April 2012. The decision made by the Committee was subsequently reported in Issue No. 31 of Drug News. In December 2012, the Committee discussed the issue of the use in patients with prosthetic heart valves, and decided that the sales pack label and/or package insert of the products should include wordings such as “the safety and efficacy of dabigatran has not been studied in patients with prosthetic heart valves. Therefore, use of dabigatran is not recommended in these patients”. In view of the latest recommendations on the contraindicated use in these patients, the issue will be further discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

EU: New safety recommendations minimise the risk of gas embolism during spray applications of fibrin sealants

CHMP of EMA made a number of risk-minimisation measures for the fibrin sealants Evicel and Quixil as reported in Issue No. 37 of Drug News. On 14 December 2012, CHMP had further recommended instructions for other fibrin sealants Tisseel, Tissucol, Artiss and Beriplast P to optimise the safe use of these medicines when applied as spray during surgery. The review of fibrin sealants was initiated following reports of gas embolism with Evicel and Quixil in association with the use of spray devices. These events appeared to be related to the use of the spray device at higher-than-recommended pressures and/or in closer-than-recommended proximity to the tissue surface. CHMP concluded that the risk of gas embolism with Tisseel, Tissucol and Artiss (though low) could not be excluded, and thus recommended that the product information of these medicines be updated. These included:

- the product information should be updated with clear and consistent advice for healthcare professionals regarding recommended pressure and distance to use during spraying application;
- the marketing-authorisation holders for these medicines should ensure that they were used with pressure regulators that did not exceed the maximum pressure required to deliver the fibrin sealant, and that they contained labels stating the recommended pressure and distance; and
- the product information should include a warning that the risk of gas embolism appeared to be higher when fibrin sealants were sprayed using air, as compared to CO_2, and patients should be closely monitored for signs of gas embolism.

For Beriplast P, as the product did not require a gas -assisted spray device during application, there was no risk of gas embolism when it was used in accordance with prescribing advice and with the recommended device.

In Hong Kong, "Tisseel" is registered as Tisseel Kit (1 ml: HK-38346, 2ml: HK-38347, 5ml: HK-38348); Tisseel Lyo powders and solvents for fibrin sealant (1ml: HK-58061, 2ml: HK-58298), Tisseel solution for fibrin sealant (2ml: HK-58015, 4ml: HK-58014 and 10ml: HK-57908), and Tisseel Lyo Inj (HK-58943). "Beriplast P" is registered as Beriplast P Combi-Set (1ml: HK-48635, 3ml: HK-48636). All 11 products are prescription medicines indicated as supportive treatment for improvement of haemostasis in surgery where standard surgical techniques are insufficient. In view of the EMA's recommendations, a letter to healthcare professionals was issued on 17 December 2012, and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board. "Tissicol" and "Artiss" are not registered pharmaceutical products in Hong Kong.

EU / Singapore: Review of Tredaptive, Pelzont and Trevaclyn

On 21 December 2012, EMA announced that a review of the safety and efficacy of Tredaptive, Pelzont and Trevaclyn, identical medicines indicated for the treatment of dyslipidaemia was in process. The review was triggered because EMA was informed by Merck, Sharp & Dohme (MSD) of the preliminary results of a large, long-term study comparing the clinical effects of these medicines in combination with statins therapy and statin alone. The study raised questions about the efficacy of the medicines when added to statins treatment, as this did not reduce the risk of major vascular events compared with statin therapy alone. In addition, a higher frequency of non-fatal but serious side effects was seen in patients taking both medicines than in patients only taking statins. EMA's Pharmacovigilance Risk Assessment Committee (PRAC) would assess the data and make a recommendation to CHMP, which would issue an opinion on the regulatory action required. While the review was ongoing, EMA recommended that no new patients should be started on treatment with these medicines or enrolled in clinical trials involving these medicines. Patients currently using Tredaptive, Pelzont or Trevaclyn should not stop their treatment.

On 27 December 2012, Health Sciences Authority of Singapore also announced that MSD would like to inform healthcare professionals in Singapore the

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findings in the HPS2-THRIVE study of Tredaptive (results as mentioned above). Given the current understanding of these new data and until additional analyses could be completed, physicians were advised not to start new patients on Tredaptive. It was not necessary at this time to stop Tredaptive in patients who were currently using the therapy.

In Hong Kong, Tredaptive (ER Niacin/Laropiprant) 1g/20mg Tab (HK-57317) is registered by MSD (Asia) Ltd. and is a prescription medicine indicated for the treatment of combined dyslipidaemia and primary hypercholesterolaemia when not controlled by diet & exercise alone. In view of the above recommendations, a letter to healthcare professionals was issued on 24 December 2012, and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board. On 21 January 2013, the Department of Health (DH) endorsed the total recall of Tredaptive (ER Niacin/Laropiprant) 1g/20mg Tab from the market by MSD (Asia) Ltd. "Pelzont" and "Trevaclyn" are not registered pharmaceutical products in Hong Kong.

Drug Recall

Total recall of Fusen E.M. Cap 100mg (HK-49463)

On 10 December 2012, DH endorsed a licensed drug wholesaler, Hitpharm Pharmaceutical Co Ltd. (Hitpharm), to recall from the market all batches of Fusen E.M. Cap 100mg, because of quality issues. Fusen E.M. Cap 100mg is an over-the-counter medicine containing aspirin, which is an antithrombotic indicated for the prevention of embolism.

Through DH's market surveillance programme, DH was informed by the Government Laboratory samples from one batch (lot number: 012015) of Fusen E.M. Cap 100mg was found to contain less than the labelled quantity of the active ingredient (about 80%). The samples had also failed the dissolution test. As a precautionary measure, Hitpharm decided to recall all batches of the product from the market.

The product had been supplied to pharmacies, medicine companies and registered medical practitioners as well as exported to Macau. DH had alerted the concerned parties about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports in connection with the product. A press statement was released on the same day to alert the public of the recall.

The quality defect could affect the effectiveness of the product. Thus, healthcare professionals and retailers should stop supplying the said product to their clients. People who had used the affected product should consult healthcare providers if in doubt or feeling unwell.

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 is a $10,000 fine and three months' imprisonment.

Batch recall of animal drug Quantel Tablet (Vet) (HK-50424)

On 17 December 2012, DH instructed a licensed drug wholesaler, C Vetapet & Co. (C Vetapet), to recall from the market one batch of an animal drug, namely Quantel Tablet (Vet) (lot number: C28083), because of a quality issue. Quantel Tablet, containing fenbendazole and praziquantel, is an over-the-counter drug indicated for the treatment of roundworms and tapeworms in dogs and cats.

The recall was initiated because the product's manufacturer, Chanelle Pharm. Manuf. Ltd. in Ireland found out a batch had failed the dissolution test during the stability study. According to the manufacturer, the assessment revealed that the failure was probably due to the higher than average tablet hardness of the batch concerned. The failure in the dissolution test may affect the efficacy of the product.

Drug Recall

According to C Vetapet, a total of 15,000 boxes of the batch concerned were imported into Hong Kong in June 2012. The product was only supplied to local pet shops. DH had closely monitored the recall. A press statement was released on the same day to alert the public of the recall.

Members of the public should consult veterinary surgeons if in doubt.

Total recall of Panadol Suspension 120mg/5ml (HK-52694)

On 18 December 2012, DH instructed a licensed drug wholesaler, GlaxoSmithKline Ltd. (GSK), to recall from shelves all Panadol Suspension 120mg/5ml (in 60ml bottles) due to incorrect labelling. Panadol Suspension 120mg/5ml is an over-the-counter medicine indicated for the relief of pain and fever in children.

Upon investigation of a complaint from a member of the public, DH found that the bottle label of Panadol Suspension 120mg/5ml was printed with the wrong Chinese translation of the active ingredient content. "120mg of acetaminophen contained in every 5ml (1 teaspoonful)" was wrongly translated with a reference to "120ml of acetaminophen". This error in the description only appeared on the bottle label.

Panadol Suspension 120mg/5ml is registered by GSK and distributed by LF Logistics (HK) Ltd. According to GSK, about 110,000 bottles of the affected product had been imported into Hong Kong since June 2011. The product was supplied to local pharmacies and medicine stores as well as 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 reports in connection with the product. A press statement was released on the same day to alert the public of the recall. Members of the public should consult healthcare professionals if in doubt.

Drug Incident

Persons arrested for illegal sale of unregistered pharmaceutical products with controlled drug ingredients

On 7 December and 12 December 2012, joint operations were conducted by DH and the Police resulting in the arrests of a 43-year-old man for suspected illegal sale of Proloonging Delay Spray for men, and a 30-year-old man for suspected illegal sale of Geftinat 250mg Tablets. DH issued press statements on the days of operations.

For both cases, complaints were received alleging the unregistered pharmaceutical products were offered for sale on the Internet. Investigation revealed that the products were not pharmaceutical products registered with the Pharmacy and Poisons Board of Hong Kong and contained substances which are Part I poisons.

For the former case, Proloonging Delay Spray for men contained the drug ingredient lidocaine, which is a Part I poison and should be sold at pharmacies under the supervision of registered pharmacists. Lidocaine is commonly used as a local anaesthetic to relieve pain or to desensitise skin before minor operations. Common side effects include hypersensitive reaction.

For the latter case, Geftinat 250mg Tablets contained the drug ingredient gefitinib, which is a Part I poison and should be sold at pharmacies under the supervision of registered pharmacists. Gefitinib is a prescription drug used for the treatment of lung cancer. A subsequent search of a nearby premises rented by the man further revealed other unregistered pharmaceutical products containing Part I poisons erlotinib, dasatinib, sorafenib tosylate, imatinib and lenalidomide, which are all oncology medications.

Members of the public should consult healthcare professionals for advice before taking any medications for their conditions, particularly for treatment of cancers.

Pet shop raided for selling unregistered pharmaceutical product with controlled drug ingredient

On 20 December 2012, a joint operation was conducted by DH and the Police in a pet shop resulting in the arrest of a 42-year-old saleswoman

for illegal sale of an unregistered pharmaceutical product called Heartgard Plus Tablets.

Upon the investigation of a complaint from a member of the public, DH found two unregistered animal drugs, namely Heartgard Plus Tablets and Tri-Heart Plus Tablets, both containing the antibiotic ivermectin inside the pet shop in Wan Chai. Hong Kong pharmaceutical product registration number was not found on the products label. Both products are indicated for the prevention of heartworm disease and treatment of other parasite infections in dogs. They are both prescription drugs and should be used under the advice and instructions of veterinary surgeon.

In addition, the pet shop's head office located in Tsuen Wan was also raided. Apart from the above two products, another two unregistered animal drugs, namely Frontline Plus for Dogs and Frontline Plus for Cats, were found. Both Frontline Plus products, containing fipronil, are over-the-counter animal drugs indicated for the treatment of fleas and ticks in dogs or cats.

Members of the public should only use antibiotics for their pets under the advice and instructions of a veterinary surgeon. They should consult a veterinary surgeon for advice if in doubt.

DH issued press statement on the day of operation.

Warning on slimming product with banned drug ingredients

On 11 December 2012, DH appealed to members of the public not to buy or consume a slimming product named "Green Portfolio" 「綠色組合」as it may contain undeclared and banned drug ingredients that are dangerous to health.

Through DH's market surveillance programme, "Green Portfolio" was found to be offered for sale in an Internet auction website. Laboratory test on the product sample revealed that the product was found to contain trace amount of sibutramine and phenolphthalein.

Sibutramine is a Part I poison and was once used as an appetite suppressant. Since November 2010, products containing sibutramine have been banned because of an increased cardiovascular risk. Phenolphthalein was once used for treating constipation but has been banned for its possible cancer-causing effect.

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

Warning on oral product with banned drug ingredient

On 14 December 2012, DH appealed to members of the public not to buy or consume an oral product called "Jin Tan 1-Ching-Sung Laxative Tablets"「金壇一輕鬆通便片」, as it may contain a banned drug ingredient that is dangerous to health.

DH was notified by Hospital Authority about a 92-year-old male patient who was hospitalized for management of mild confusion. It was found that he had the history of using "Jin Tan 1-Ching-Sung Laxative Tablets" labelled as containing banned drug diacetyldiphenolisatin (also known as oxyphenisatin) for constipation for a few years. The patient purchased the product from a local medicine shop in Central. DH commenced investigation immediately and during the investigation, a 61 year-old male was arrested by the Police for sale of unregistered pharmaceutical product.

Diacetyldiphenolisatin was banned for its hepatotoxicity in Hong Kong in 1997. It was used previously for treating constipation.

This was the second incidence of the same product this year and the previous news was reported in Issue No. 32 of Drug News.

Patients with constipation and any chronic disease ought to consult healthcare professionals for appropriate advice and management. They are strongly urged to refrain from self-medication or using over-the-counter products without professional supervision.

Drug Incident

A product containing any western drug ingredient must be registered under the Pharmacy and Poisons Ordinance before it can be sold in Hong Kong. Part I poisons such as lidocaine must not be sold on Internet. They must be sold at registered pharmacy by a registered pharmacist or under his or her supervision. Possession or sale of unregistered pharmaceutical product and possession or sale of Part I poison are offences under the Pharmacy and Poisons Ordinance (Cap 138). The maximum penalty is a $100,000 fine and two years' imprisonment for each offence. Possession or illegal sale of antibiotics are also offences under the Antibiotics Ordinance (Cap 137) and the maximum penalty is a $30,000 fine and one year's imprisonment for each offence.

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 products mentioned in the above incidents were not registered pharmaceutical products under 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. They should stop using the aforementioned products immediately if they had them in their possession and to consult healthcare professionals if they felt unwell after taking the products. The products should be destroyed or disposed properly, or submitted to the Department's Drug Office during office hours.

News in Brief

1, 3-Dimethylamylamine put under control as pharmaceutical product

On 5 December 2012, the Registration Committee of the Pharmacy and Poisons Board decided to regulate 1, 3-Dimethylamylamine (DMAA) as pharmaceutical product with effect from 1 April 2013, after considering the pharmacological effects of DMAA, its potential risk of causing adverse effects and the international situations in the control of DMAA.

Therefore, DMAA must be registered as pharmaceutical product with the Pharmacy and Poisons Board before they can be legally sold in Hong Kong. Any person who sells, offers for sale or distributes or possesses for the purposes of sale, distribution or other use any unregistered pharmaceutical product is liable to prosecution. The maximum penalty is a fine of $100,000 and two years' imprisonment. So far, no product containing DMAA has been registered in Hong Kong.

DMAA was first synthesized as a nasal decongestant in 1940s. It can narrow the blood vessels and elevate blood pressure, leading to cardiovascular events ranging from shortness of breath to heart attack. DMAA containing products had been banned or removed from the market by overseas health authorities including the United States, the United Kingdom, New Zealand, Finland, Canada and Australia. DMAA is found in some body building supplements and weight loss products such as "Jack3d".

Wholesalers and retailers must stop selling or distributing "Jack3d" and other DMAA containing products and remove them from shelves and market. DH will prosecute traders for illegal possession of DMAA containing products for sale or distribution.

Members of the public should not buy nor use "Jack3d" and other DMAA containing products. They should consult healthcare professionals for advice if they feel unwell after using the products.

Useful Contact

Drug Complaint:

Tel: 2572 2068
Fax: 3904 1224
E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920
Fax: 2186 9845
E-mail: adr@dh.gov.hk
Link: http://www.drugoffice.gov.hk/adr.html
Post: ***Pharmacovigilance Unit,***
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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.