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, Canada: Premature termination of a clinical trial with Doribax (doripenem) in ventilator-associated pnuemonia (VAP) due to significant safety concerns

On 3 January 2012, Janssen Pharmaceuticals, Inc. announced to terminate a clinical trial with Doribax (doripenem) because the interim data showed a higher mortality rate and lower clinical cure rate among ventilator-assoicated pneumonia (VAP) subjects receiving a 7-day course of doripenem (1g every 8 hours) compared with those treating with a 10-day course of imipenem-cilastatin (1g every 8 hours). In response, public safety annoucements were issued in different countries.

Situation in US

Doribax is not approved for any type of pneumonia or for doses greater than 500mg every 8 hours in US. The US Food and Drugs Administration (FDA) was reviewing the trial results and the Agency considered Doribax remained to be safe and effective for its approved indications (adults with complicated intra-abdominal infections and complicated urinary tract infections) and at its recommended dose and regime (500mg every 8 hours intravenously, given over 1 hour, for 5-14 days).

Situation in Canada

Treatment of adults with nosocomial pneumonia, including VAP, at a regime of a 1 or 4 hour intravenous infusion of 500mg every 8 hours for 7-14 days is one of the approved indications in Canada. Janssen Inc. would be working with Health Canada to include the information about the risk identified from the study in the Product Monograph.

In Hong Kong, Doribax for Inj 500mg (HK-57638) is registered by Johnson & Johnson (HK) Ltd. and is a prescription medicine. VAP is one of the approved indications with the recommended dose of 500 mg every eight hours intravenously, given over 1 or 4 hours (which is half the dose used in the clinical trial being terminated). This dose and indication is also approved in other drug regulatory authorities such as European Medicines Agency (EMA), the UK Medicines and Healthcare products Regulatory Agency (MHRA) and Therapeutic Goods Administration (TGA). Department of Health (DH) issued a letter on 6 January 2012 to inform healthcare professionals about the risk. DH will keep vigilant against any updated safety news of the drug from other drug regulatory authorities.

Canada: Conclusion on the safety review of the smoking-cessation drug Champix

Subsequent to the previous announcement made by Health Canada on 17 June 2011 as reported in Issue No. 21 of Drug News, Health Canada announced on 19 January 2012 that the review of Champix was complete. After evaluating the data from a quit-smoking clinical trial involving 700 smokers with cardiovascular disease who were treated with Champix or placebo, Health Canada considered that the small study size and some design weaknesses made it impossible to conclude the cardiovascular safety of Champix. The drug labelling for Champix had been updated to include a more detailed description of the study and findings, along with precautions for patients on cardiovascular safety. Patients were advised to consult their health professionals for queries and seek immediate medical attention if they developed suspicious symptoms of a heart attack or stroke. Public were reminded that smoking was a major known risk factor for cardiovascular disease and smoking

cessation posed a great benefit to patients with cardiovascular disease.

In Hong Kong, Champix (varenicline) Tab 0.5mg and 1mg are registered by Pfizer Corporation HK Ltd. and are prescription medicines indicated for smoking-cessation. A letter to healthcare professionals has been issued on 17 June 2011 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 (the Registration Committee) of the Pharmacy and Poisons Board.

EU, Canada: Safety precautions to prevent administration errors with Velcade (bortezomib)

Since the authorization of Velcade in 2004, EMA noticed that there were three fatal cases of accidental intrathecal administration of Velcade in the EU where the medicine was only authorized to be given via intravenous route. The involved patients were found to be receiving intrathecal chemotherapy in addition to Velcade. In this connection, EMA's Committee for Medicinal Products for Human Use (CHMP) issued an announcement on 19 January 2012 to remind healthcare professionals and recommend specific precautionary measures to prevent further occurrence of this administration error. In Canada, Janssen Inc., also alerted healthcare professionals regarding the above issue on 26 January 2012.

The precautionary measures included:

- Different connectors should be used for intrathecal and intrevaenous medicines if possible.
- Administration of intrathecal and other parenteral chemotherapy should be scheduled at a different time if possible.
- Syringes should be labelled with the name of the medicine and its route of adminstration.
- The labelling of syringes should be checked twice before administration.
- Healthcare professionals involved in administering or managing the chemotherapy should be well trained and informed of the risk of intrathecal administration of Velcade.

In Hong Kong, three pharmaceutical products Velcade for Inj 3.5mg (HK-53329), Velcade for Inj 1mg (HK58055) and Velcade for Inj 3.5mg (France) (HK-60429) are registered by Johnson & Johnson (Hong Kong) Ltd. and are prescription medicines. Velcade is used in targeted cancer therapy for the treatment of multiple myeloma and mantle cell lymphoma and is only approved to be administered intravenously. DH was informed by Johnson & Johnson regarding the matter on 16 January 2012 and a letter to healthcare professionals was then issued on the same day. DH will keep vigilant against any updated safety news of the drug.

EU: Suspension of marketing authorizations for meprobamate-containing medicines due to the risk of serious side effects

On 20 January 2012, EMA recommended the suspension of all marketing authorisations for oral meprobamate-containing medicines in the EU, because their risks, especially the risk of serious neurological side effects, were greater than their benefits.

After reviewing the safety and efficacy of these medicines from all available sources, including studies, post-marketing surveillance, the published literature and poison control centres, CHMP noted that there was a risk of serious and potentially fatal side effects, such as coma, in patients taking meprobamate-containing medicines under normal use. The small difference between the therapeutic and harmful dose made it more vulnerable to have accidental overdose and thus further aggravated these risks. CHMP also noted that the additive nature of meprobamate could lead to serious and sometimes fatal side effects on abrupt cessation of long-term treatment.

CHMP had recommended to withdraw the medicines from the market gradually, within 15 months of the European Commission decision, to allow the prescribers to find appropriate treatments for their patients. Doctors were advised to stop prescribing meprobamate-containing medicines over the next 15 months and consider alternative treatments in accordance to the national clinical recommendations. Patients currently taking the medicines were advised to discuss with their doctor about the treatment plan at their next routine appointment.

Safety Update

In Hong Kong, Meprobamate Tablet 400mg (HK-30318), the only pharmaceutical product containing meprobamate, is registered by Christo Pharm Ltd. It is a prescription medicine and is used as an anxiolytic agent. A letter to healthcare professionals was issued on 21 January 2012 and the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

US: Recall of Swanson Ultra Softgels Q Gel Mega 100

25 January 2012 - Swanson Health Products, Inc. recalled Swanson Ultra Softgels Q Gel Mega 100, 60 softgels from the US market as the product contained undeclared soy lecithin instead of the sunflower lecithin reflected in the ingredient statements. The lot under recall was 189588 and the manufacturer was Tishcon Corp., Westbury, NY.

'Tishcon Q-Gel Mega Softgel Cap' (HK-57538) contains Vitamin E (as d-alpha tocopherol) and Q-Gel Coenzyme Q-10. In Hong Kong, it is registered by Rejuvenis International Ltd. According to the company, the above batch had not been imported to Hong Kong .

Drug Recall

Batch recall of Allopurinol-Teva Tablets 100mg (HK-57739)

On 16 January 2012, DH instructed a licensed drug wholesaler, the International Medical Co. Ltd. (International) to recall from shelf a batch of Allopurinol-Teva Tablets 100mg (batch number: 1580211) on quality ground as black substances were found on some tablets in two blisters of the product. Allopurinol-Teva contains allopurinol and is indicated mainly for hyperuricaemia and gout. It can be sold in pharmacies under the supervision of a pharmacist.

DH received notification from the Hospital Authority (HA) on 14 January 2012 that black substances were found on some tablets of the product. Report from the Government Laboratory revealed that the black substances, which adhered on the surfaces of some tablets, bore similar features as used hydrocarbon oil. Hydrocarbon oil might be used in equipment for the production of tablets. The investigation showed the black substances were only found on a few tablets of the affected batch and could be due to quality issues.

According to International, the affected batch was manufactured by Teva Pharmaceutical Works Private Ltd Co. in Hungary. A total of 22,965 boxes had been imported into Hong Kong and were supplied to HA hospitals, local pharmacies and private doctors. DH had alerted HA hospitals and professional healthcare bodies about the matter and closely monitored the recall. DH had not received any adverse event report in connection with the product. Press statement was issued on the same day.

Batch recall of Diurex tablets (HK-51628)

On 18 January 2012, DH instructed a licensed drug manufacturer, Vickmans Laboratories Ltd. (Vickmans), to recall from shelf a batch of Diurex tablets (batch number: 110738) in view of a quality defect report. Diurex contains frusemide which is used for the management of hypertension. It is a prescription medicine which can only be sold under the supervision of a pharmacist on presentation of a doctor's prescription at a dispensary.

DH came to learn of the problem while investigating a public complaint about the detection of a plastic fragment embedded in a Diurex tablet. So far, this appeared to be an isolated event. There was no indication that other batches were affected.

The batch of Diurex tablets was manufactured in Hong Kong in June 2011. A total of 783 boxes of 500 tablets were supplied to various HA hospitals, private doctors and pharmacies. DH had alerted HA hospitals and professional healthcare bodies about the matter and closely monitored the recall. DH had not received any adverse event report in connection with the product. Press statement was issued on the same day.

Public are advised to examine the above products before consumption. If in doubt, they should seek advice from their healthcare professionals.

Selling any drug not of the nature, substance or quality demanded by the purchaser is an offence contravened 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 Recall

Batch recall of Saridon Tablet (HK-24091)

On 19 January 2012, DH endorsed a licensed drug wholesaler, Bayer Healthcare Limited (Bayer), to recall from consumers a batch of Saridon Tablet (batch number: CM01474) because of a packaging error. Some boxes labelled as 20-tablet were actually 10-tablet packs. Saridon Tablet contains paracetamol, propyphenazone and caffeine. It is an over-the-counter medicine for the relief of pain and fever.

Bayer revealed that the affected batch was manufactured in Indonesia. A total of 61,701 boxes of the affected batch had been sold to local retailers since September 2011. DH closely monitored the recall and had not received any adverse event report in connection with the product. Press statement was issued on the same day.

Selling any drug with a container falsely describes the drug is an offence contravened the Public Health and Municipal Services Ordinance (Cap 132). The maximum penalty involved is $50,000 and six months' imprisonment.

Drug Incident

Warning on slimming products found with banned drug ingredients

In January 2012, DH appealed to the public not to buy or consume two slimming products called "CanSui" 「纖秀塑形纖維素」and "FAT 2 AND 1 BURNERS III" 「全新三代超脂肪燃燒彈二合一搭擋軟膠囊加硬膠囊」as they were found to contain banned drug ingredients sibutramine and phenolphthalein that may cause serious side effects.

For the former case, DH was notified by the HA about a 20-year-old lady who was hospitalized on 26 December 2011 because of acute psychosis. She described a history of consumption of a slimming product called "CanSui", which was purchased from the Internet. Analysis on the product sample by the Government laboratory detected sibutramine and phenolphthalein. Drug-related psychosis was suspected and she was discharged from hospital on 29 December 2011 after treatment.

For the latter case, it was discovered through DH's surveillance programme that the slimming product, "FAT 2 AND 1 BURNERS III", was offered again for sale on the Internet. DH immediately purchased the product from the internet for laboratory analysis and the results by the Government Laboratory confirmed that the product contained sibutramine and phenolphthalein. In May 2011, DH first discovered the product was offered for sale on an Internet auction site. DH had ordered the removal of the product from the Internet and also exhorted members of the public to stop using the product. Since then, the product was not found by DH surveillance programme until the surveillance in January 2012.

Sibutramine is a Part I poison and was once a western medicine used as an appetite suppressant. Since November 2010, products containing sibutramine had been banned by the Pharmacy and Poisons Board because of the increased cardiovascular risk.

Phenolphthalein is another banned drug. It was used previously for treating constipation, but had been banned for its cancer-causing effect.

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

Press statements related to the two cases were issued.

Warning on orally consumed product containing banned and undeclared drug ingredients

On 11 January 2012, DH appealed to members of the public not to buy or consume an oral product, "Tang Bao Kou Fu Yi Dao Su Jiao Nang" 「糖保口服胰島素膠囊」, as it had been found to contain three undeclared western drugs, one of which is a banned item in Hong Kong.

DH was notified by the HA about a 69-year-old man with diabetes mellitus who admitted to hospital on 26 December 2011 because of dizziness, nausea and vomiting. He had a history of consuming the above product. Investigation found that he suffered from hypoglycemia and renal failure. The product was purchased via a website outside Hong Kong. Analysis on the product sample by the Government

Drug Incident

Laboratory detected metformin, glibenclamide and phenformin. He was discharged from hospital on 30 December 2011 after treatment.

Metformin and glibenclamide are western drug ingredients used for management of diabetes. Their side effects include anorexia, nausea, vomiting, diarrhea and lactic acidosis for metformin, and nausea and gastro-intestinal upset for glibenclamide.

Phenformin is also a hypoglycaemic agent, but it had been banned in Hong Kong since 1985 because of the potential fatal effect of lactic acidosis.

Metformin and glibenclamide are Part I poisons. Under the Pharmacy and Poisons Ordinance, products containing them can only be sold with a doctor's prescription and under the supervision of a pharmacist.

Patients with chronic medical illness which requires holistic long term management ought to consult healthcare professionals for appropriate advice on medication. They are strongly urged not to self-medicate or use over-the-counter medication without professional supervision. Diabetic patients should not self-manage their blood sugar with product claimed to treat diabetes. The consequences can be serious. People who have taken the above product should consult their healthcare providers immediately because the product may cause life-threatening hypoglycemia and lactic acidosis.

Press statement related to the case was issued.

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.

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. A product containing any western drug ingredient must be registered under the Ordinance before it can be sold in Hong Kong. Under the Pharmacy and Poisons Ordinance, possession or sale of unregistered pharmaceutical product and possession or sale of Part I poison are offences with each of them liable to the maximum penalties of a $100,000 fine and two year's imprisonment. 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 that contained undeclared western drug ingredients and they should see doctors if they feel unwell after using 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:

You are encouraged to report any suspected or confirmed ADR cases to our office by:

Tel: 2319 2920

Fax: 2147 0457

E-mail: adr@dh.gov.hk

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

News in brief

Commencement of the Undesirable Medical Advertisements (Amendment) Ordinance 2005 to regulate health claims of orally consumed products

The Secretary for Food and Health has appointed June 1, 2012 to be the commencement date of the provisions related to the control of health claims of orally consumed products under the Undesirable Medical Advertisements (Amendment) Ordinance 2005. The Commencement Notice has been published in the gazette on January 13, 2012.

The Undesirable Medical Advertisements Ordinance (Cap 231) (UMAO) was first enacted in 1953 with the purpose of protecting public health through prohibiting/restricting advertisements which may induce the seeking of improper management of certain health conditions. Under the UMAO, advertisements likely to lead to the use of any medicine, surgical appliance or treatment for the purpose of treating human beings for, or preventing them from contracting listed diseases or conditions or purposes specified in different Schedules of the Ordinance are not allowed.

In view of the ever increasing number of orally consumed products with various health claims on the local market and stakeholders' concern about their impact on public health, the Administration amended the UMAO in June 2005 after careful risk assessment and consultation. The major amendments included:

(1) adding a whole new Schedule 4 on prohibiting/ restricting six groups of health claims by orally consumed products (Table 1),

(2) increasing the penalty for contravention of UMAO from $10,000 to level 5[1] and imprisonment for six months for a first offence; and from $25,000 and imprisonment for one year to level 6[1] and imprisonment for one year for a second or subsequent offence,

(3) empowering the Director of Health to appoint inspectors to enforce the Ordinance, and

(4) amendments to Schedules 1 and 2.

Provisions related to amendments in Schedule 1 and 2 had been implemented since January 2006. The commencement date for the rest of the amendments was proposed to be June 1, 2012 because amongst the latter, there was reliance on the Chinese Medicine Ordinance (Cap 549) which only came into full implementation from December 1, 2011.

The Department of Health (DH) has been launching various education and publicity activities for stakeholders since 2005. In particular, a set of guidelines on the Amendment Ordinance has been prepared for the trade and briefings and seminars have been organised to provide platforms for interactive communication between stakeholders and the regulatory authority. For details of the UMAO, the Amendment Ordinance and the guidelines on the Amendment Ordinance, please refer to the website of Drug Office -

http://www.drugoffice.gov.hk/eps/root/en/pharmaceutical_trade/other_useful_information/umao.html

[1] The maximum penalties for level 5 and level 6 are $50,000 and $100,000 respectively.

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.