Drug News
藥 物 情 報

Issue Number 57

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in July 2014 with relevant information update before publish. 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

Singapore / UK: Transdermal Durogesic® (fentanyl): reminder on the potential for life-threatening harm from accidental exposure to transdermal fentanyl

It was noted from the website of Health Sciences Authority (HSA) on 4 July 2014 that Janssen, a division of Johnson & Johnson Pte Ltd., alerted healthcare professionals to the potential risk of accidental exposure to transdermal Durogesic® patches. The issue of accidental exposure is not a new safety issue. However, cases of accidental exposure to transdermal Durogesic® in non-patch wearers, leading to fatal outcomes especially in children, continue to be reported overseas. To prevent potential life-threatening harm from accidental exposure to Durogesic® patches, healthcare professionals are reminded of the importance to provide clear information to patients and caregivers regarding risk of accidental patch transfer, accidental ingestion of patches by children, and need for appropriate disposal of used patches.

On 21 July 2014, the Medicines and Healthcare Products Regulatory Agency (MHRA) announced people using fentanyl skin transdermal patches and their carers should check that the patches are stuck on securely and are disposed of safely. The MHRA has received three reports of accidental contact with or transfer of fentanyl patches to date. Two of the three reports concerned children. People using fentanyl patches are reminded that the used patch should be folded in half so that the adhesive side sticks firmly to itself. It should then be safely thrown away in a secure bin so that it is not picked up by young children. If a patch is transferred to another person, remove it and get medical help immediately. If a patch is swallowed, get medical help immediately.

A European review assessed the risks of accidental exposure (including accidental transfer and improper disposal) associated with these patches. As a result, the product information for people who use these patches and healthcare professionals will be updated to strengthen these warnings and stress the importance of keeping the patches out of reach and sight of children.

In Hong Kong, there are six registered pharmaceutical products containing fentanyl transdermal patches, namely Durogesic Transdermal Patch 50mcg/h (HK-53753), 100mcg/h (HK-53754), 25mcg/h (HK53755), 12mcg/h (HK-53883), Fentanyl HPO Transdermal Patch 50mcg/h (HK-59083), and 25mcg/h (HK-59084). All the products are prescription only medicines. Related news had been released by the US Food and Drug Administration (FDA) and Health Canada, and were reported in Drug News Issues No. 30 and 47. A letter to healthcare professionals to draw their attention and urge them to report any adverse drug reactions (ADR) related to the drug was issued on 20 April 2012. So far, the Department of Health (DH) has not received any local adverse drug reaction report related to these products. In view of the above MHRA's announcement, 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. The DH will keep vigilant on any further safety update related to fentanyl transdermal patches by other drug regulatory authorities.

Singapore: Limitations on use of Ventolin® (salbutamol sulphate) for inhibition of premature labour

It was noted from the website of HSA on 4 July 2014 that GlaxoSmithKline in Singapore informed healthcare professionals of important restrictions regarding the use of oral and parenteral Ventolin® in the treatment of premature labour. Obstetric use of short-acting beta-agonists (SABA), including salbutamol sulphate, is associated with serious, sometimes fatal, adverse cardiovascular events in both the mother and the foetus or new-born. Oral salbutamol sulphate should not be used in the treatment of premature labour and the use of parenteral salbutamol sulphate should be limited to inhibition of premature labour between the 22nd and 37th weeks of gestation for a maximum of 48 hours and administered with close monitoring of both mother and foetus. In addition, parenteral salbutamol sulphate should not be used in women with a history of heart disease or in any conditions where prolongation of the pregnancy is hazardous to the mother and foetus. The local package insert for oral Ventolin® has been updated with the removal of the obstetric indication while the local package insert for parenteral Ventolin® is in the process of being strengthened to include additional recommendations for screening and monitoring during management of premature labour. The above revisions to the prescribing information for both oral and parenteral administration of Ventolin® do not alter the prescribing information regarding the use of Ventolin® for respiratory indications, including pregnant women.

In Hong Kong, there is one registered pharmaceutical product containing injectable salbutamol, namely Ventolin Soln for IV Infusion 1mg/ml (HK-02796). It is a prescription only medicine and is registered by GlaxoSmithKline Ltd (GSK). GSK has already updated the packet insert to include the above safety information. So far, the DH has not received any local adverse drug reaction report related to the product. In view of the above HSA's announcement, a letter to healthcare professionals to draw their attention and urge them to report any ADR related to the drug was issued on 4 July 2014. The DH will keep vigilant on any safety update related to the product by other drug regulatory authorities.

EU: PRAC recommends restricted use of bromocriptine for stopping breast milk production

On 11 July 2014, the European Medicines Agency (EMA) had completed an EU-wide review of bromocriptine-containing medicines for preventing or suppressing lactation in women after childbirth. The Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has recommended that the medicines only be used for this purpose (in strengths up to 2.5 mg) when there are compelling medical reasons for stopping lactation, such as to avoid further distress after loss of the baby during or just after childbirth, or in mothers with HIV infection, who should not breastfeed. Bromocriptine should not be used routinely for preventing or stopping milk production, nor to relieve symptoms of pain or swelling of the breasts after childbirth. Such symptoms can be managed by measures such as breast support or applying ice, and the use of painkillers if needed.

The review of bromocriptine was carried out at the request of the French medicines authority (ANSM) following concerns in France over increased reports of rare but potentially serious or fatal side effects, particularly cardiovascular side effects, neurological side effects such as seizures and psychiatric side effects. ANSM considered that the risk of these events was not acceptable since lactation is a natural process that eventually stops if the infant is not breastfed, and other means of management are available.

The PRAC recommendation will now be forwarded to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) which will adopt a final position.

In Hong Kong, there are seven registered pharmaceutical products containing bromocriptine which are prescription only medicines. So far, the DH has not received any local adverse drug reaction report related to the drug. In view of the above announcement by the EMA, a letter to healthcare professionals draw their attention and urge them to report any ADR related to the drug was issued on 14 July 2014. The DH will remain vigilant on any safety updates of the drugs and actions taken by overseas regulatory authorities and the final legally binding decision by the European Commission for further consideration.

Canada: Possible cardiovascular problems associated with testosterone products

On 15 July 2014, Health Canada advised patients and healthcare professionals of new safety information regarding testosterone hormone replacement products and a risk of serious and possibly life-threatening cardiovascular problems.

Testosterone hormone replacement products are used in men who are experiencing medical conditions because their body cannot make enough testosterone. Health Canada has recently completed a safety review on testosterone replacement products. This review found a growing body of evidence (from published scientific literature and case reports received by Health Canada and foreign regulators) for serious and possible life-threatening heart and blood vessel problems such as heart attack, stroke, blood clot in the lungs or legs; and increased or irregular heart rate with the use of testosterone replacement products. Health Canada is working with manufacturers to update the Canadian product labels regarding this risk.

In Hong Kong, there are eight registered pharmaceutical products containing testosterone which are prescription only medicines. Related news on the risks of cardiovascular events and venous thromboembolism had been released by FDA and were reported in Drug News Issues No. 52 and 56 respectively. A letter to healthcare professionals to draw their attention and urge them to report any ADR related to the drug was issued on 20 June 2014. So far, the DH has not received any adverse drug reaction report on the drug. In view of the above Health Canada's announcement, another letter to healthcare professionals was issued on 16 July 2014, and the matter will be discussed in the meeting of the Registration Committee. The DH will remain vigilant on any safety updates related to the drug and actions taken by other overseas regulatory authorities.

EU / UK: Levonorgestrel and ulipristal remain suitable emergency contraceptives for all women, regardless of bodyweight

On 24 July, 2014, the EMA has concluded its review of emergency contraceptives containing levonorgestrel or ulipristal acetate to assess whether increased bodyweight affects the effectiveness of these medicines in preventing unintended pregnancy following unprotected sexual intercourse or contraceptive failure. The Agency's Committee for Medicinal Products for Human Use (CHMP) recommends that these emergency contraceptives can continue to be used in women of all weights as the benefits are considered to outweigh the risks.

In November 2013, following a national procedure, the product information of one emergency contraceptive containing levonorgestrel, Norlevo, was updated on the basis of results from two clinical studies to state that Norlevo is less effective in women weighing 75 kg or more and not effective in women weighing more than 80 kg. An EU-wide review was then started to assess whether similar information should be included in the product information for other emergency contraceptives that contain levonorgestrel, and for ellaOne, an emergency contraceptive that contains ulipristal acetate.

Having assessed all the available evidence on the effectiveness of emergency contraceptives, the CHMP considered that the data available are too limited and not robust enough to conclude with certainty that contraceptive effect is reduced with increased bodyweight, as stated in the product information for Norlevo. For levonorgestrel-containing products, some clinical studies have suggested a reduced effectiveness in women with high bodyweight, but in others no trend for a reduced effect with increasing bodyweight was observed. Similarly, for ulipristal acetate, although limited data from clinical trials suggest a possible trend for a reduced contraceptive effect, the data are too limited and insufficiently precise to draw definite conclusions. The CHMP recommended that the results of these studies should be included in the product information of emergency contraceptives, but that the current statements on the impact of bodyweight in the product information for Norlevo should be deleted.

The CHMP recommendation will now be sent to the European Commission for a legally binding decision that will be valid throughout the EU.

On the same day, the UK MHRA announced that the EMA had concluded its review of emergency contraceptives containing levonorgestrel or ulipristal acetate to assess whether the effectiveness of Levonelle (containing levonorgestrel) and ellaOne (containing ulipristal acetate) was reduced

with increased body weight. They concluded that based on the data available the benefits of using these emergency contraceptives remains positive and it cannot be concluded that body weight has an impact on the effectiveness of these widely used medicines.

In Hong Kong, there are 29 registered emergency contraceptive medicines containing levonorgestrel and 2 containing ulipristal acetate. All are prescription only medicines. News related to concerns on increased bodyweight affects the effectiveness of the emergency contraceptive medicines had been released by EMA and Health Canada, and were reported in Drug News Issues No. 52 and 53. Letter to healthcare professional has been issued on 27 March 2014 to draw their attention on Health Canada's announcement on warning of reduced effectiveness of emergency contraceptives in women over a certain body weight. The matter is pending for discussion in the meeting of the Registration Committee. In view of the new announcement by the EMA and the MHRA that emergency contraceptives remain suitable for women regardless of bodyweight, a letter to healthcare professionals to update the new conclusion was issued on 25 July 2014, and the latest information will be provided to the Committee for consideration.

Canada: Safe use of topical antiseptics for preoperative and preinjection skin preparation

On 25 July 2014, Health Canada was reminding healthcare professionals of the safe use of topical antiseptics used to clean the skin before an operation (preoperative) or before an injection (preinjection). These products can be considered safe and effective; however, if proper care is not taken when using them, they can become contaminated and cause serious, subsequent infections.

This class of topical antiseptics is used to remove microorganisms such as bacteria or fungi on the patient's skin prior to injections or surgery. In Canada, these products are available as single-use or multi-use products, and contain ingredients such as ethyl alcohol, isopropyl alcohol, povidone-iodine, and chlorhexidine gluconate. Topical antiseptics that are sterile will be labelled as such, with the word *sterile* appearing on the label. To date, Health Canada has not received any confirmed adverse reaction reports of infection linked to the use of topical antiseptics contaminated by improper use, handling, or storage.

Healthcare professionals are reminded that:

- In-house infection control policies and procedures for proper sterile technique, use, handling and storage of topical antiseptics, should be followed;
- In the event of culturing an unusual organism in a post-procedural infection setting, contamination of antiseptics should be suspected.

In Hong Kong, there are numbers of products registered as topical antiseptics, containing ingredients such as isopropyl alcohol, povidone iodine, and chlorhexidine. They are all over-the-counter products. So far, the DH has not received any local adverse drug reaction report related to these products. The DH will keep vigilant on any safety updates of the drugs and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

Canada: Duragesic ® MAT (fentanyl transdermal system) - Introduction of a single ink colour (dark green) on all strengths of patches

On 28 July 2014, Janssen Inc., in consultation with Health Canada, informed healthcare professionals of the potential for dosing errors with changes to ink printing on the patches of Duragesic® MAT. Currently, different colours of ink in combination with the text on the patch are used to identify the different strengths of Duragesic® MAT (12, 25, 50, 75, and 100mcg/h). Current users should be aware that one shade of dark green ink, intended to enhance visibility of the patch, will now be used on all strengths. The product carton and pouch will retain the use of the multi-colour system to aid in further differentiating the various patch strengths.

There is a potential for dosing errors (overdose or underdose) with a change from the existing use of different ink colours to identify individual strengths of Duragesic® MAT patches to a single ink colour (dark green) across all strengths.

Healthcare professionals should emphasize the following points when counselling patients or caregivers on the use of Duragesic® MAT:

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- the colour of the ink printed on the Duragesic® MAT patches will change to a dark green ink regardless of patch strength;

- ink colour printed on the patch should not be used to identify patch strength upon application and removal;

- if using multiple patches, check the strength on each patch before application and removal given the change to a single ink colour for all strengths and the similarity of some actual patch sizes; and

- instructions on safe storage, handling, use and disposal to reduce the risk of accidental exposure.

In Hong Kong, there are four registered pharmaceutical products of fentanyl transdermal system manufactured by Janssen Pharmaceutica N.V. Belgium, namely Durogesic Transdermal Patch 50mcg/h (HK-53753), 100mcg/h (HK-53754), 25mcg/h (HK-53755) and 12mcg/h (HK-53883). All four products are registered by Johnson & Johnson (HK) Ltd (J&J). As confirmed by J&J and the package inserts of the products, multi-colour system is still being used in the product carton, pouch and including the patch of the four products to aid in differentiating the various patch strengths. As on 21 August 2014, J&J confirmed that there was no change to the local patch labeling and there was no intention to adopt the colour change as Canada.

Drug Recall

Recall of Hiy Gluco & Chon Plus Calcium Tablets (HK-60675)

On 11 July 2014, DH instructed a licensed drug wholesaler, Welfore Co. Ltd., to recall all batches of Hiy Gluco & Chon Plus Calcium Tablets 60 tablets/bottle and 200 tablets/bottle from the market because the sales label of the product is unapproved. Hiy Gluco & Chon Plus Calcium Tablets contains glucosamine, chondroitin and calcium which is used as a dietary supplement for joint health. The product can be sold over-the-counter without a prescription.

Upon the DH's investigation into a public enquiry, it was revealed that the sales label of the product in the market did not match with the approved version. Unapproved sales label has not been evaluated by the DH and renders the product as unregistered. The quality of product is nonetheless not affected.

According to Welfore Co. Ltd., about 3400 bottles of 60's pack and 760 bottles of 200's pack Hiy Gluco & Chon Plus Calcium Tablets have been distributed in Hong Kong since February 2013. They have been supplied to doctors, local pharmacies and drug stores. The DH will closely monitor the recall. As on 11 July 2014, the DH had not received any adverse reaction report related to the use of the product. A notice was released on the Drug Office's website on the same day to alert the public of the recall.

Batch recall of Baxter 0.9% Sodium Chloride Injection (HK-20984)

On 11 July 2014, the DH endorsed a licensed drug wholesaler, Baxter Healthcare Ltd (Baxter), to recall from the healthcare sector one batch (batch number: P309187) of 0.9% Sodium Chloride Injection (50ml) due to particulate matter found in the product. 0.9% Sodium Chloride Injection is indicated as a source of water or electrolytes for medical treatment.

The DH received notification from Baxter today that the manufacturer in the United States (US) was conducting a voluntary recall of the affected batch globally following a complaint of particulate matter found in one packet of the above product. Particulates, if infused, may cause blockage of blood vessels which can result in stroke, heart attack or damage to other organs such as the kidney or liver. Allergic reactions, local irritation and inflammation are also possible. No adverse events in connection with this issue have been reported.

Preliminary investigation by the manufacturer in the US indicated that the particulate matter might have been introduced into the product during the production of the plastic container. So far, there is no evidence to suggest that other batches of the product were affected.

According to Baxter, 49 cartons (each with 96 packets) of the affected batch have been supplied to the Hospital Authority, private hospitals and private

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doctors. The DH will closely monitor the recall. As on 11 July 2014, the DH had not received any adverse reaction report related to the use of the product. A notice was released on the Drug Office's website on the same day to alert the public of the recall.

Healthcare providers should visually inspect for any particulate matter before using the product and other injectable drugs. If particulates or suspicious matters are found, they should immediately stop using it and report the case to the supplier.

Drug Incident

Public urged not to buy or consume two slimming products with undeclared and banned drug ingredient

On 14 July 2014, the DH appealed to members of the public not to buy or consume two slimming products, namely Slim Perfect Arm and Slim Perfect Legs, as they contained an undeclared and banned drug substance.

Acting on a public complaint, samples of the products concerned were obtained from a retail shop in Yau Ma Tei for analysis. Analytical results from the Government Laboratory revealed that the slimming products contained sibutramine, a banned drug ingredient.

A joint operation was conducted by the DH and the Police on the same day, in which an 18-year-old woman was arrested for suspected illegal sale and possession of an unregistered pharmaceutical product and Part I poison.

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

Members of the public who have purchased the above products should stop consuming them immediately. They should consult healthcare professionals for advice if feeling unwell or in doubt after consuming them.

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

Man arrested for suspected illegal sale of slimming product with undeclared and banned drug substance

On 30 July 2014, a joint operation by the DH and the Police resulting in the arrest of a 40-year-old man for illegal sale of a slimming product named Dr. Mao Slimming Capsules, which is suspected to contain an undeclared and banned drug substance.

Previously, during the DH's surveillance programme, a sample of the above slimming product was purchased through the Internet for analysis. Test results from the Government Laboratory revealed that the product contained sibutramine.

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

Members of the public who have purchased the above product should stop consuming it immediately. They should consult healthcare professionals for advice if feeling unwell or in doubt after consumption.

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

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 should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part I poisons and unregistered pharmaceutical products are offences under the Pharmacy and Poisons Ordinance (Cap 138). The maximum penalty is a fine of $100,000 and two years' imprisonment for each offence.

All registered pharmaceutical products should carry a Hong Kong registration number on the package in the format of "HK-XXXXX". The products mentioned in the above incidents were not registered pharmaceutical products under the 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

Deregistration of rectal suppository containing domperidone 10mg

On 9 July 2014, the DH made press release to draw the public's attention to the decision of the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee (the Registration Committee) of the Pharmacy and Poisons Board to deregister a rectal suppository containing domperidone 10mg with effect from 1 October, 2014, because the benefits of the product no longer outweigh its risks.

The Registration Committee's decision was made at its meeting on 7 July 2014, after taking into consideration the findings from overseas studies and the usage information of the product in Hong Kong.

Domperidone, taken orally or as a rectal suppository, is generally used as an antiemetic agent for the short-term treatment of nausea and vomiting.

The Registration Committee noted that domperidone in certain doses is clearly associated with a small increased risk of potentially life-threatening effects on the heart while data supporting the effectiveness of domperidone 10mg rectal suppositories are limited. Hence, the Registration Committee decided to deregister a rectal suppository containing domperidone 10mg with effect from 1 October, 2014.

In Hong Kong, there is currently one registered rectal suppository containing domperidone 10mg, namely Domper Suppository 10mg (HK-42477), which is a non prescription medicine. The DH had issued letters to inform healthcare professionals of the Registration Committee's decision to deregister the product, and to advise them to arrange suitable alternative treatment for their patients.

As for oral products containing domperidone, the Registration Committee has recommended that local drug manufacturers and wholesalers should strengthen the products' information on dosage and indication according to the recommendations of overseas regulatory authorities.

When the Registration Committee's decision takes effect on 1 October 2014, all drug wholesalers, retailers and healthcare professionals must stop selling or supplying the rectal suppository containing domperidone 10mg. The wholesalers concerned are also required to recall the product from the market by 30 September 2014. The DH will take enforcement action against any illegal possession or sale of such a product afterwards.

Under the Pharmacy and Poisons Ordinance (Cap 138), illegal sale or possession for the purpose of sale of unregistered pharmaceutical products are both criminal offences. The maximum penalty for each offence is a fine of $100,000 and two years' imprisonment.

Doctors and pharmacies should stop prescribing or dispensing the rectal suppository containing domperidone 10mg. Patients using the product are advised to consult their healthcare professionals to review their treatment plans as soon as possible.

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,***
Drug Office, Department of Health,
Rm 1856, 18/F, Wu Chung House,
213 Queen's Road East,
Wan Chai, Hong Kong

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.