Drug News
藥物情報

Issue Number 96

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in October 2017 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

Canada: Mannitol as a non-medicinal ingredient in medications for pregnant women

On 13 October 2017, Health Canada announced that Health Canada is aware of recent concerns around the use of mannitol as a non-medicinal ingredient in medications for use by pregnant women. Health Canada would like to assure Canadians that, based on its evaluation of the evidence available, consumption of small quantities of sugar substitutes, including mannitol, during pregnancy does not pose a health risk.

Mannitol is a type of sugar commonly used as a non-medicinal ingredient in medications, such as tablets or capsules, to help in the manufacture of the product. Non-medicinal ingredients are evaluated for safety. They are used, for example, to help hold a tablet together or give it colour.

Mannitol has a long history of safe consumption in many products commonly used and consumed by pregnant women, including folic acid supplements, vitamins, candy and baked goods.

Health Canada assesses all medications, including generic medications, for safety, quality and effectiveness before authorizing them for sale in Canada. This includes assessing scientific evidence for the safety of non-medicinal ingredients, as well as carefully considering whether clinical trial data appropriately supports authorization of the medication for specific populations, such as pregnant women.

Pregnant women should speak to their health professional if they have questions about medications they are taking. Health Canada continues to monitor the safety of authorized medications once they are on the market in Canada.

In Hong Kong, mannitol is commonly used as an excipient (not an active ingredient) in pharmaceutical products. The Department of Health (DH) should remain vigilant on any similar safety update of the concerned excipient from other drug regulatory agencies.

UK: Gabapentin (Neurontin): risk of severe respiratory depression

On 26 October 2017, the Medicines and Healthcare products Regulatory Agency (MHRA) of United Kingdom (UK) announced that a European review of gabapentin was triggered by reports of patients developing respiratory depression without concomitant use of opioids. This reaction has already been recognised with concomitant use of gabapentin with opioids. Having considered the available evidence from worldwide spontaneous reports and in the literature, the review recommended that the product information for gabapentin should be amended to include warnings for severe respiratory depression (frequency rare; may affect up to 1 in 1,000 patients post-marketing).

The patient leaflet that accompanies gabapentin is being updated to include warnings about breathing problems, which if severe may need emergency and intensive care. The leaflet advises patients to seek medical help if they experience any trouble breathing or are taking shallow breaths.

MHRA also reminded that when prescribing

gabapentin in patients who require concomitant treatment with opioid medicines, patients should be carefully observed for signs of central nervous system (CNS) depression, such as somnolence, sedation, and respiratory depression, and the dose of either gabapentin or the opioid should be reduced appropriately.

In UK, there have been 50 Yellow Card reports of respiratory depression or dyspnoea associated with gabapentin between 19 February 1996 and 1 September 2017. Of these cases, 17 report opioids as co-suspect or concomitant medications.

Healthcare professionals are advised:
- to be aware of the risk of CNS depression, including severe respiratory depression, with gabapentin; and
- to consider whether dose adjustments might be necessary in patients at higher risk of respiratory depression, including elderly people, patients with compromised respiratory function, respiratory or neurological disease, or renal impairment, and patients taking other CNS depressants.

In Hong Kong, there are 24 registered pharmaceutical products containing gabapentin. All are prescription-only medicines. As on 13 November 2017, DH has not received any case of adverse drug reaction (ADR) related to gabapentin. In view of the above MHRA's announcement, DH issued a letter to inform local healthcare professionals to draw their attention on the above safety information on 27 October 2017 and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board (the Registration Committee).

UK: Isotretinoin (Roaccutane): rare reports of erectile dysfunction and decreased libido

On 26 October 2017, MHRA of UK announced that a routine European Union (EU) review showed that some patients taking isotretinoin had reported sexual dysfunction adverse effects, including erectile dysfunction and decreased libido. One possible mechanism for this effect may be through a reduction in plasma testosterone levels. The review recommended that sexual dysfunction including erectile dysfunction and decreased libido should be added to the list of side effects in the product information. The package leaflet for patients will include “Problems getting or maintaining an erection and lower libido” as possible side effects.

In UK, MHRA has received 14 Yellow Card reports of sexual dysfunction associated with isotretinoin between the beginning of 1985 and 7 September 2017. In the same time period, there have been 49 reports of erectile or ejaculation dysfunction, and 23 reports of decreased or loss of libido associated with isotretinoin. MHRA estimates that over the past few years, around 30,000 patients (male and female) per year have been treated with isotretinoin.

MHRA also reminded that rare reports of depression, exacerbated depression, anxiety, aggressive tendencies, mood alterations, and psychotic symptoms in association with isotretinoin treatment. Very rarely, suicidal ideation, suicide attempts, and death by suicide have been reported. Particular care should be taken in patients with a history of depression. Monitor all patients for signs of depression and refer for appropriate treatment if necessary. Further psychiatric or psychological evaluation may be necessary after discontinuation of treatment with isotretinoin.

Healthcare professionals are advised:
- to be aware of reports of sexual side effects, including erectile dysfunction and decreased libido, in patients taking oral isotretinoin, indicated for severe acne; and
- the exact incidence of these adverse reactions is unknown but considering the number of patients in UK taking the medicine, reports are understood to be rare.

In Hong Kong, there are 11 registered pharmaceutical products containing isotretinoin. All are prescription-only medicines. As on 13 November 2017, DH has received 2 cases of ADR related to isotretinoin, but these cases were not related to sexual dysfunction, including erectile dysfunction and decreased libido, or mood disorders. In view of the above MHRA's announcement, DH issued a letter to inform local healthcare professionals to draw their attention on the above safety information on 27 October 2017 and the matter will be discussed by the Registration Committee.

Drug Recall

DH endorsed recall of Frontline Spot On Cats Solution 50mg (HK-49992), Frontline Spot On Dogs Solution 67mg (HK-49993), 134mg (HK-49995) and 268mg (HK-49994)

On 3 October 2017, DH endorsed a licenced pharmaceutical secondary packaging manufacturer, Skylite Limited (Skylite), to recall the following batches of products from the market because the products' labels do not match with the registered ones.

Product Name	Batch Number	Hong Kong Registration Number
Frontline Spot On Cats Solution 50mg	R20503CW	HK-49992
Frontline Spot On Dogs Solution 67mg	R20112AX	HK-49993
Frontline Spot On Dogs Solution 268mg	R20205AR	HK-49994
Frontline Spot On Dogs Solution 134mg	M23130BX	HK-49995

During DH routine inspection, it was found that the labels of the above products were different from the registered labels, which render the products unregistered. Since the supply of unregistered pharmaceutical products contravenes the Pharmacy and Poisons Regulations (Cap. 138A), Skylite voluntarily recalls the products from the market.

The above products, containing fipronil, are used on cats or dogs for killing fleas. According to Skylite, the products had been supplied to local pet shops and veterinary clinics.

A notice was posted on the Drug Office website on 3 October 2017 to alert the public of the product recall.

Drug Incident

DH raided retail stall for suspected illegal sale and possession of unregistered medicines

On 3 October 2017, DH and the Police conducted a joint operation and raided a retail stall in Sham Shui Po for suspected illegal sale and possession of unregistered pharmaceutical products and possession of unregistered proprietary Chinese medicine (pCm).

Acting upon intelligence, samples of products offered for sale in the stall were purchased for analysis. Test results from the Government Laboratory confirmed that four of the samples contained undeclared Part 1 poisons and were found to be unregistered pharmaceutical products. These products are:

	Product Name	Part 1 Poisons Found
1.	九毒王藏药乳膏 (no English name)	Clobetasol propionate and miconazole
2.	ZANG YAO XUAN DU WANG CAO BEN RU GAO	Clobetasol propionate and miconazole
3.	MIAO JIA DU XUAN GAO	Clobetasol propionate and miconazole
4.	藏宫秘宝点磁透骨贴 (no English name)	Diclofenac

The product suspected to be an unregistered pCm was called 百痛油 (no English name) while four other products were suspected to be unregistered pharmaceutical products.

During the operation, a 60-year-old man and a 40-year-old woman were arrested by the Police for suspected illegal sale and possession of Part 1 poisons, unregistered pharmaceutical products and possession of unregistered pCm.

Clobetasol propionate is a steroid substance for treating inflammation. Inappropriate or excessive application of steroids could cause skin problems and body-wide side effects like moon face, high blood pressure, high blood sugar, muscle atrophy, adrenal insufficiency and osteoporosis. Products containing clobetasol propionate should be used under a doctor's directions and be supplied in a pharmacy under supervision of a registered pharmacist upon a doctor's prescription. Miconazole is used for the treatment of fungal infections with side effects including local irritation and sensitivity reactions. Diclofenac is used for the relief of pain and common side effects of using diclofenac-containing analgesic patches include itching and rash at the site of application.

A notice was released on the website of Drug Office on 3 October 2017 to alert the public of the drug incident.

DH urged public not to buy or consume slimming product with undeclared controlled ingredient N-desmethylsibutramine

On 16 October 2017, DH urged the public not to buy or consume a slimming product named MEIXING as it was found to contain an undeclared controlled ingredient.

Acting upon a public enquiry, DH collected a sample of the above product for analysis. Test results from the Government Laboratory confirmed that the sample contained N-desmethylsibutramine.

N-desmethylsibutramine is structurally similar to sibutramine, and both of them are Part 1 poisons under the Pharmacy and Poisons Ordinance (Cap 138). Sibutramine was once used as an appetite suppressant. Since November 2010, products containing sibutramine have been banned in Hong Kong because of increased cardiovascular risk. N-desmethylsibutramine is expected to pose similar health risks.

The public may visit the Drug Office's pages for health messages on weight control and slimming products (www.drugoffice.gov.hk/eps/do/en/consumer/slim.html) and information on products found to contain undeclared Western medicines (www.drugoffice.gov.hk/eps/specMedsNews/slimming/en/consumer).

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 notice was released on the website of Drug Office on 16 October 2017 to alert the public of the drug incident.

DH raided retail stall for suspected illegal sale of unregistered pharmaceutical products

On 17 October 2017, DH and the Police conducted a joint operation and raided a retail stall in Sham Shui Po for suspected illegal sale of unregistered pharmaceutical products, which were found to contain undeclared controlled ingredients.

Acting upon intelligence, samples of products were purchased previously from the above stall for analysis. Test results from the Government Laboratory confirmed that samples of the following three products contained undeclared Part 1 poisons:

	Product Name	Part 1 Poisons Found
1.	Zang Yao Xuan Du Wang Cao Ben Ru Gao	Clobetasol propionate and miconazole
2.	Qi Du Zang Wang Gao	Clobetasol propionate
3.	Xie Wang Jin Gu Leng Fu Tie	Diclofenac

During the operation, a 35-year-old man was arrested by the Police for suspected illegal sale and possession of Part 1 poisons and unregistered pharmaceutical products.

Clobetasol propionate is a steroid substance for treating inflammation. Inappropriate or excessive application of steroids could cause skin problems and body-wide side effects like moon face, high blood pressure, high blood sugar, muscle atrophy, adrenal insufficiency and osteoporosis. Products containing clobetasol propionate should be used under a doctor's directions and be supplied in a pharmacy under the supervision of a registered pharmacist upon a doctor's prescription. Miconazole is used for the treatment of fungal infections with side effects including local irritation and sensitivity reactions. Diclofenac is used for the

relief of pain and common side effects of using diclofenac-containing analgesic patches include itching and rash at the site of application.

A notice was released on the website of Drug Office on 17 October 2017 to alert the public of the 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 1 poisons should be sold at registered pharmacies under the supervision of registered pharmacists. Illegal sale or possession of Part 1 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. Antibiotics can only be supplied at registered pharmacies by registered pharmacists or under their supervision and upon a doctor's prescription. They should only be used under the advice of a doctor. Illegal sale or possession of antibiotics are offences under the Antibiotics Ordinance (Cap 137) and the maximum penalty is a $30,000 fine and one year's 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.

Update on Drug Office's website: You can now search the newly registered medicines in the past year at http://www.drugoffice.gov.hk/eps/drug/newsNRM60/en/healthcare_providers?pageNoRequested=1.
Details of ALL registered pharmaceutical products can still be found in the Drug Office website at http://www.drugoffice.gov.hk/eps/do/en/healthcare_providers/news_informations/reListRPP_index.html.

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: 2319 6319

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.