Drug News
藥 物 情 報

Issue Number 89

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

EU: EMA reviewing cancer medicine docetaxel

On 10 March 2017, the European Medicines Agency (EMA) of European Union (EU) is investigating the cancer medicine docetaxel following cases of neutropenic enterocolitis in patients in France, most of whom were being treated for operable breast cancer. Neutropenic enterocolitis is a serious inflammatory condition of the intestine associated with neutropenia (low levels of neutrophils, a type of white blood cell that fights infection). It is a known and rare side effect of docetaxel (which may affect up to one in 10,000 people).

A preliminary assessment by EMA's Pharmacovigilance Risk Assessment Committee (PRAC) indicates that the frequency of this side effect has not increased in the last two years. A thorough evaluation of available data is being carried out and final conclusions will be published once the review is completed.

Docetaxel is an important therapeutic option which has been shown to extend the lives of cancer patients. While the review is ongoing, EMA advises that doctors should continue to prescribe this medicine according to recommendations in the current product information, including detailed recommendations for the prevention and management of neutropenia.

Patients who have any questions about their treatment should speak to their doctor.

Docetaxel is a medicine used for the treatment of several types of cancer, including breast cancer. It has been authorized in the EU since 1995 under several trade names including Taxotere.

The review of docetaxel is being carried out in the context of a safety signal. A safety signal is information on a new or incompletely documented adverse event that is potentially caused by a medicine and that warrants further investigation.

The review is being carried out by PRAC, the committee responsible for the evaluation of safety issues for human medicines. Once the review is completed, PRAC will make any recommendations necessary to minimize risks and protect patients' health.

In Hong Kong, there are twenty-eight registered pharmaceutical products containing docetaxel. All these products are prescription only medicines. As on 7 April 2017, the Department of Health (DH) has received nine cases of adverse drug reactions (ADR), but none of them were related to neutropenic enterocolitis. DH will remain vigilant on the conclusion of the review and any safety updates from other overseas drug regulatory authorities.

Canada: KEYTRUDA (pembrolizumab) - Risk of severe skin reactions: Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

On 20 March 2017, Health Canada advised that cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), some with fatal outcomes, have been reported in patients treated with KEYTRUDA (pembrolizumab). Health Canada is currently working with the manufacturer

to include this safety information in the Canadian Product Monograph.

KEYTRUDA is a programmed death receptor-1 (PD-1) blocking antibody. In Canada, it is indicated for the treatment of patients with unresectable or metastatic melanoma who have not received prior treatment with ipilimumab. KEYTRUDA is also authorized in Canada under the notice of compliance with conditions (NOC/c) policy for the treatment of patients with:

- unresectable or metastatic melanoma and disease progression following ipilimumab therapy and, if BRAF V600 mutation positive, following a BRAF or MEK inhibitor.
- metastatic non-small cell lung carcinoma (NSCLC) whose tumours express PD-L1 (as determined by a validated test) and who have disease progression on or after platinum-containing chemotherapy.

The potential risk of SJS and TEN with KEYTRUDA use was evaluated using currently available safety data from the published literature and the manufacturer's global safety database (which includes both clinical trial serious adverse events and post-marketing reports). One fatal case of SJS in a clinical trial and one fatal case of TEN in the post-marketing setting have been reported internationally in patients treated with KEYTRUDA. Including these cases, there have been 8 cases of SJS (6 in clinical trials, and 2 in post-marketing) and 2 cases of TEN (both in post-marketing). Of these 10 reports, one case of SJS was reported in Canada. Two of the 10 reports had a temporal association with KEYTRUDA use, had few confounding factors, and had skin biopsies that were consistent with SJS or TEN. Approximately 11,000 patients in clinical trials and 27,000 patients in the post-marketing setting have been treated with KEYTRUDA.

Patients are advised that SJS and TEN are serious life-threatening conditions that often involve wide areas of the skin, the eyes, and lining of the mouth, nose, throat, or genital area. Flu-like symptoms including fever, tiredness, muscle and joint pain are seen early which are followed by a widespread rash and reddening and blistering of the skin and moist lining of the mouth, nose, throat, or genital area. This often leads to peeling and shedding of the affected skin which looks like a severe burn. Patients should seek immediate medical attention if they experience any of these symptoms.

Health Canada reminds healthcare professionals to:

- advise patients about the benefits and risks of KEYTRUDA, including the risk and early symptoms of SJS and TEN.
- suspend KEYTRUDA treatments if SJS, TEN or other severe skin reaction signs or symptoms (Grade 3) occur and refer the patient for immediate specialized evaluation and treatment.
- permanently discontinue KEYTRUDA, if SJS or TEN is confirmed.

In Hong Kong, Keytruda Solution for Injection 100mg/4ml (HK-64228) and Keytruda Powder for Injection 50mg (HK-64229) are pharmaceutical products registered by Merck Sharp & Dohme (Asia) Ltd, and are prescription only medicines. As on 7 April 2017, DH has received 13 cases of ADR in connection with pembrolizumab, of which one case was related to TEN. In view of the above Health Canada announcement, DH issued a letter to inform local healthcare professionals to draw their attention on the Health Canada announcement on 21 March 2017, and the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

US: FDA alerts consumers of nationwide voluntary recall of EpiPen and EpiPen Jr

On 31 March 2017, the U.S. Food and Drug Administration is alerting consumers to the Meridian Medical Technologies' voluntary recall of 13 lots of Mylan's EpiPen and EpiPen Jr (epinephrine injection) Auto-Injector products used for emergency treatment of severe allergic reactions. This recall is due to the potential that these devices may contain a defective part which may result in the devices' failure to activate. The recalled product was manufactured by Meridian Medical Technologies and distributed by Mylan Specialty.

While the number of reported failure is small, EpiPen products that potentially contain a defective part are being recalled because of the potential for life-threatening risk if a severe allergic reaction goes untreated. Consumers should keep and use their current EpiPens if needed until they get a

replacement.

As stated on the product label, consumers should always seek emergency medical help right away after using their EpiPens, particularly if the device did not activate.

At this time, the 13 lots identified, distributed between 17 December 2015, and 1 July 2016, are the only EpiPen lots impacted by the U.S. recall. Consumers who have EpiPens from lots that are not included in this recall, do not need to replace their EpiPen prior to its expiration date.

Product/Dosage	NDC Number	Lot Number	Expiration Date
EpiPen Jr Auto-Injector, 0.15 mg	49502-501-02	5GN767	April 2017
EpiPen Jr Auto-Injector, 0.15 mg	49502-501-02	5GN773	April 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	5GM631	April 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	5GM640	May 2017
EpiPen Jr Auto-Injector, 0.15 mg	49502-501-02	6GN215	September 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM082	September 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM072	September 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM081	September 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM088	October 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM199	October 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM091	October 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM198	October 2017
EpiPen Auto-Injector, 0.3 mg	49502-500-02	6GM087	October 2017

In Hong Kong, Epipen and Epipen Jr are not registered pharmaceutical products. According to the DH records, Epipen 0.15mg and 0.3mg have been imported from U.S. for the treatment of particular patients by Luen Cheong Hong Ltd (LCH). LCH confirmed that the affected batches in the U.S. FDA announcement have not been imported into Hong Kong. DH will monitor the development of the situation and will continue to liaise with other importers of Epipen products to provide timely update of the situation when necessary.

Drug Recall

DH endorsed recall of Cinotec Cream 0.005% (HK-40871) and 0.0125% (HK-40873)

On 22 March 2017, DH endorsed a licensed pharmaceutical manufacturer, Medipharma Ltd, to recall all batches of Cinotec Cream 0.005% (HK-40871) and 0.0125% (HK-40873) from the market due to a quality issue.

Following the previous recall of five batches of the above two products reported on 3 August 2016, more samples were collected for analysis. Test results from Government Laboratory revealed that the content of active ingredient of some batches of the two products was lower than that claimed on the label.

As a precautionary measure, Medipharma suspended the manufacturing of the two products since the last recall. In view of the latest test results, the manufacturer decided to recall all batches of the two products from the market. Investigations revealed that inadequate mixing in the manufacturing process might have led to non-uniformity of the content of the active ingredient. The products under recall might have reduced efficacy in relieving symptoms but should pose no harmful effects to patients. Members of the public using the two products should consult their healthcare providers if in doubt or when symptoms persist.

Cinotec Cream, containing fluocinolone acetonide, is a steroid cream and is a prescription medicine for the treatment of eczema and allergic skin disorders. According to Medipharma, the two products have been supplied to Hospital Authority, DH clinics, private doctors and pharmacies.

Related news was previously posted on DH website on 3 August 2016, and was reported in Drug News Issue No. 82. As on 7 April 2017, DH has not received any ADR report in connection with the two products. A notice was posted on the Drug Office website on 22 March 2017 to alert the public of the drug recall.

Drug Incident

DH urges public not to buy or consume product with undeclared controlled ingredient desmethyl fondenafil

On 1 March 2017, DH urged the public not to buy or consume a product called Eromate Coffee as it was found to contain an undeclared Part 1 poison.

During DH's market surveillance, a sample of the above product was purchased for analysis. Test results from Government Laboratory confirmed that the sample contained desmethyl fondenafil, a Part 1 poison.

DH officers initiated a joint operation with the Police immediately and a woman aged 40 was arrested by the Police for illegal sale and possession of Part 1 poison in an operation on 1 March 2017.

Desmethyl fondenafil is structurally similar to sildenafil, a prescription drug ingredient used for erectile dysfunction, and this undeclared ingredient may interact with nitrates found in some drugs such as nitroglycerin and may cause decrease in blood pressure to dangerous levels.

Drug Office has market surveillance in place to monitor drug safety. Drug Office will continue to monitor the safety of virility products by intelligence collection, investigations and laboratory analysis.

The public may visit the Drug Office's webpage on health message on sexual dysfunction and virility products and those found to contain undeclared Western medicines for more information.

A notice was posted on the Drug Office website on 1 March 2017 to alert the public of the drug incident.

DH urges public not to buy or use two external products with undeclared controlled ingredients clobetasol proprionate and miconazole

On 13 March 2017, DH appealed to the public not to buy or use two external products, namely Great

Taste Aloe Skin cream EXCELLCENT EFFECT and Great Taste Aloe Skin cream FULL EFFECT, as they were found to contain undeclared controlled ingredients.

Acting upon intelligence, DH purchased samples of the above products from the market for analysis. The test results from Government Laboratory revealed that both samples contained Part 1 poisons, clobetasol proprionate and miconazole. Products containing clobetasol proprionate and miconazole should only be sold at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription.

DH initiated investigation immediately and seized the above products from the seller for further analysis.

Clobetasol proprionate is a steroid substance. 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. Miconazole is used for the treatment of fungal infection with side effects such as local irritation and sensitivity reactions.

A notice was posted on the Drug Office website on 13 March 2017 to alert the public of the drug incident.

DH urges public not to buy or consume product with undeclared controlled ingredient dexamethasone

On 23 March 2017, DH urged the public not to buy or consume a product called TONIK TUAN HAJI 1921 as it was found to contain an undeclared Part 1 poison.

Acting upon intelligence, a sample of the above product was purchased for analysis. Test results from Government Laboratory confirmed that the sample contained dexamethasone, a Part 1 poison.

Dexamethasone is a steroid and its side-effects include moon face, high blood pressure, high blood sugar, muscle atrophy, adrenal insufficiency and even osteoporosis. Products containing dexamethasone are prescription medicines which should only be used under the advice of a medical doctor.

A notice was posted on the Drug Office website on 23 March 2017 to alert the public of the drug incident.

DH urges public not to buy or consume product with undeclared controlled ingredient sildenafil

On 30 March 2017, DH urged the public not to buy or consume a product called VENERGY CAPSULE 100mg as it was found to contain an undeclared Part 1 poison.

During DH's market surveillance, a sample of the above product was purchased for analysis. Test results from Government Laboratory confirmed that the sample contained sildenafil, a Part 1 poison.

DH officers initiated an investigation immediately and seized a quantity of the above product.

Sildenafil is a prescription drug used for erectile dysfunction and should be taken under doctor's advice and supplied at pharmacies under the supervision of a registered pharmacist upon a doctor's prescription. Side effects of sildenafil include low blood pressure, headache, vomiting, dizziness and transient vision disturbances. It may interact with some drugs (such as nitroglycerin for the treatment of angina) and cause a decrease in blood pressure to dangerous levels. Improper use of sildenafil may pose serious health risks, especially for patients with heart problems.

The public may visit the Drug Office's webpage for health message on sexual dysfunction and virility products for more information.

A notice was posted on the Drug Office website on 30 March 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
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Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920
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E-mail: adr@dh.gov.hk
Link: http://www.drugoffice.gov.hk/adr.html
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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.