Drug News
藥 物 情 報

Issue Number 101

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in March 2018 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: Prostate cancer medicine Xofigo must not be used with Zytiga and prednisone/ prednisolone. Ongoing clinical study shows an increased risk of death and fractures with the combination.

On 9 March 2018, the European Medicines Agency (EMA) of the European Union (EU) has recommended contraindicating the use of the prostate cancer medicine Xofigo (radium-223 dichloride) with Zytiga (abiraterone acetate) and prednisone/prednisolone, due to an increased risk of death and fractures with this combination.

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has reviewed the preliminary data from an ongoing clinical study in metastatic prostate cancer patients. In this study 34.7% of patients treated with Xofigo, Zytiga and prednisone/prednisolone have died so far, compared with 28.2% of patients given placebo, Zytiga and prednisone/prednisolone.

Fractures have also occurred more frequently with the Xofigo combination than the placebo combination (26% versus 8.1%).

In view of the seriousness of the events reported, PRAC has taken action by introducing a contraindication as a temporary measure to protect patients' safety while an in-depth review of the benefits and risks of Xofigo is ongoing.

Healthcare professionals in EU must not use a combination of Xofigo with the anti-androgen Zytiga and prednisone/prednisolone, and should stop this combination in men currently treated with it and review the treatment for these patients. Healthcare professionals are also warned that the safety and efficacy of Xofigo in combination with a class of medicines called second generation androgen receptor antagonists, such as Xtandi (enzalutamide), have not been established.

These are temporary measures until the ongoing in-depth review of the benefits and risks of Xofigo is complete. EMA will communicate further at the conclusion of the review.

In Hong Kong, Xofigo Solution for Injection 1100 KBq/mL (HK-64332) is a pharmaceutical product containing radium-223 dichloride which is registered by Bayer Healthcare Ltd, and is a prescription-only medicine. Related news was previously issued by EMA, the Medicines and Healthcare products Regulatory Agency (MHRA) of the United Kingdom (UK) and the Health Sciences Authority (HSA) of Singapore, and was reported in the Drug News Issue No. 98. As on 6 April 2018, the Department of Health (DH) has received 11 cases of adverse drug reaction (ADR) related to Xofigo, but none of them are related to death and fractures. DH will remain vigilant on the development of the issue and safety update of the drug issued by other overseas drug regulatory authorities.

Singapore: Risk of serious neurologic adverse events, including encephalopathy, associated with cefepime particularly in patients with renal impairment who received doses that exceeded the recommendations

On 13 March 2018, HSA announced that Bristol-Myers Squibb would like to inform healthcare professionals of cases of serious neurologic adverse

events, including encephalopathy, that have been reported in patients with renal impairment (creatinine clearance ≤ 50 ml/min) treated with cefepime. Most of these cases had occurred in patients with renal impairment who had received dosages above the recommended, especially in elderly patients. Although the events of neurotoxicity were generally reversible upon cefepime treatment discontinuation and/or haemodialysis, some cases had a fatal outcome. Healthcare professionals are reminded to consider dosage adjustments according to the renal function status of patients who are treated with cefepime.

In Hong Kong, there are 15 registered pharmaceutical products containing cefepime and are prescription-only medicines. Related news was previously issued by the United States (US) Food and Drug Administration (FDA), and was reported in the Drug News Issue No. 32. DH issued a letter to inform local healthcare professionals to draw their attention to the risk of non-convulsive status epilepticus in patients not receiving renal dosage adjustment of cefepime on 27 June 2012. As on 6 April 2018, DH has not received any case of ADR in connection with cefepime.

On 27 February 2013, the Registration Committee of the Pharmacy and Poisons Board decided that the sales packs and/or package inserts of pharmaceutical products containing cefepime should be updated to include safety warnings on the risk of non-convulsive status epilepticus associated with cefepime. Furthermore, all registered pharmaceutical products containing cefepime have already been updated the relevant safety information of serious neurologic adverse events, including encephalopathy and non-convulsive status epilepticus in the sales packs and/or package inserts. In light of the above HSA's announcement, DH will remain vigilant on the safety update of the drug issued by other overseas drug regulatory authorities.

Australia: Duro-K 600mg potassium chloride tablets: lead content may exceed regulatory guidelines

On 15 March 2018, the Therapeutic Goods Administration (TGA) of Australia advised consumers and health professionals that TGA is aware that one batch of Duro-K 600mg potassium chloride tablets that has been supplied in Australia has higher levels of lead than permitted under new regulatory guidelines.

Following testing to comply with a new regulatory guidelines that came into effect in December 2017, the sponsor, Novartis, notified TGA that Duro-K potassium chloride 600mg tablets and Slow-K potassium chloride 600mg tablets may exceed the new maximum oral permitted daily exposure (PDE) for lead, which is 5 micrograms.

TGA then tested samples from each of the batches of Duro-K and Slow-K tablets that were being supplied in Australia. Of these samples, only one batch of Duro-K exceeded the new PDE for lead. However, that batch was compliant with the limit set by the previous guidelines, which was in effect at the time of manufacture. Novartis has also confirmed they no longer hold supply of this batch.

TGA also tested two other potassium chloride products, Span-K and Chlorvescent, which are sponsored by a different company. The lead content in these two products was within acceptable limits.

TGA has determined that the lead content in the affected batch of Duro-K does not present a significant health risk, even for people taking the maximum dose (12 tablets per day).

The PDE for lead in the new regulatory guidelines is based on the paediatric population, who absorb more lead than adults and are more sensitive to the toxic effects of lead. Duro-K tablets are not indicated for use in children.

As of 13 March 2018, there have been no reports of adverse events relating to exposure to lead associated with Duro-K in Australia.

It should be noted that lead is a known impurity that can occur due to the mining process for potassium chloride.

Based on these considerations, TGA has determined that no further action regarding the affected batch is required. However, any future batches of Duro-K and Slow-K tablets must be

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tested to ensure they comply with the new PDE for lead before they can be supplied in Australia.

In Hong Kong, Novartis Pharmaceuticals (HK) Limited (Novartis) is currently the registration certificate holder of two pharmaceutical products under the name of Slow K, i.e. Slow K Tab 600mg (HK-00200) and Slow-K Tablets 600mg (HK-62640). In December 2017, Novartis notified DH that Slow K may exceed the new ICH (International Conference for Harmonisation) guidelines for elemental impurities, i.e. when taking a high dose of Slow K, the lead intake as a result of administering the product will exceed the new guidelines.

According to Novartis, the raw materials of Slow K naturally contain lead impurities, and lead intake will not exceed the above guidelines when general therapeutic dosage (i.e. two to three tablets per day) is used. As Slow K is registered and sold in various ICH member countries, Novartis notified the drug regulatory authorities of various countries and decided to suspend the global sales of the product.

DH has continuously reviewed the requirements of ICH, and other relevant international standards and pharmacopoeias to assess the safety and quality of drugs.

In response to Novartis' notification, DH has contacted other drug suppliers to ensure local supply of the drug so that treatment of patients will not be affected. As on 6 April 2018, DH has not received any case of ADR related to potassium chloride. DH will remain vigilant on safety update of the product issued by other overseas drug regulatory authorities.

Drug Recall

DH endorsed recall of Dertec Cream (HK-62290)

On 8 March 2018, DH endorsed a licensed drug wholesaler, Mediline (Hong Kong) Company Limited (Mediline), to recall all batches of Dertec Cream (HK-62290) from the market due to a quality issue.

During DH's market surveillance, samples of the above product were collected for analysis. Testing results from the Government Laboratory revealed that the content of one of the active ingredients, namely clioquinol, was found to be less than the labelled claim, which might affect the efficacy of the product.

Mediline voluntarily recalled the product from the market and was instructed to report the root cause to DH upon investigation by the manufacturer in Thailand.

Dertec Cream, containing betamethasone, tolnaftate, gentamicin and clioquinol, is a prescription-only medicine used to treat skin inflammation and infections. According to the wholesaler, the product has been supplied to private doctors and local pharmacies.

As on 6 April 2018, DH has not received any case of ADR in connection with the above product. A notice was posted on the Drug Office website on 8 March 2018 to alert the public of the product recall.

DH endorsed batch recall of Reminyl Prolonged Release Capsules 8mg (HK-55293)

On 26 March 2018, DH endorsed a licensed drug wholesaler, Johnson & Johnson (Hong Kong) Ltd. (Johnson & Johnson), to recall one batch (Batch No.: HALDE00) of Reminyl Prolonged Release Capsules 8mg (HK-55293) from the market due to a potential quality issue.

DH received notification from Johnson & Johnson that the manufacturer of the product in Italy found that the content of active ingredient of the product was slightly less than the labeled claim during the stability testing. Since the issue might potentially affect the efficacy of the product, as a precautionary measure, Johnson & Johnson recalls the above affected batch.

The above product, containing galantamine, is a prescription medicine used for treatment of Alzheimer disease.

Drug Recall

According to Johnson & Johnson, 747 boxes (28's capsules) of the affected batch have been supplied to Hospital Authority, private hospitals, private doctors and pharmacies.

As on 6 April 2018, DH has not received any case of ADR in connection with the affected batch of product. Members of the public should consult healthcare providers if in doubt after taking the product. A notice was posted on the Drug Office website on 26 March 2018 to alert the public of the product recall.

Drug Incident

Public urged not to buy or consume virility product with doubtful composition

On 7 March 2018, DH urged the public not to buy or consume a virility product called Papapa as it was found to contain undeclared and controlled substances.

Following a public complaint, DH collected samples of the above product for analysis. Results from the Government Laboratory confirmed that the samples contained tadalafil, which is a Part 1 poison under the Pharmacy and Poisons Ordinance (Cap. 138), as well as hydroxyhomosildenafil and hydroxythiohomosildenafil.

Tadalafil is used for erectile dysfunction and should only be used under the advice of a doctor. Side effects of tadalafil 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 tadalafil may pose serious health risks, especially for patients with heart problems. Meanwhile, hydroxyhomosildenafil and hydroxythiohomosildenafil have not been proven for therapeutic use but they are expected to pose similar health risks as tadalafil.

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

A notice was posted on the Drug Office website on 7 March 2018 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

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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.