Drug News
藥 物 情 報

Issue Number 46

This is a monthly digest of local and overseas drug safety news released by the Drug Office of the Department of Health in August 2013 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: Communication on risk of eye disorders with use of Lariam® (mefloquine)

It was noted from Health Sciences Authority (HSA) website on 1 August 2013 that Roche in Singapore informed healthcare professionals of an increased risk of eye disorders including cataract, retinal disorders and optic neuropathy which may occur with latency during or after treatment with Lariam®. These eye disorders can present with visual impairment and blurred vision. This increased risk of eye disorders was based on outcomes of review of available evidence from non-clinical studies, Roche global drug safety database and published literature. Any patient on treatment with Lariam® who experiences visual disorders should be referred to his treating physician as certain conditions such as retinal disorders or optic neuropathy may require stopping treatment with the drug. The local package insert for Lariam® will be updated to reflect the new safety information.

In Hong Kong, Lariam Tab 250mg (HK-36373) is a prescription only medicine registered by Roche HK Ltd. (Roche) and is indicated for the chemoprophylaxis, therapy and stand-by treatment of malaria. Roche issued a Direct Healthcare Professional Communication about the new information for Lariam® regarding visual disturbances including optic neuropathy on 16 July 2013 and submitted the application to change the package insert by including the relevant safety information. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

US: Acetaminophen may be associated with risk of serious skin reactions

On 1 August 2013, the Food and Drug Administration (FDA) of the United States (US) announced that acetaminophen has been associated with a risk of rare but serious skin reactions. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal. These reactions can occur with first-time use of acetaminophen or at any time while it is being taken. This new information resulted from the review of the FDA Adverse Event Reporting System database and the medical literature to evaluate cases of serious skin reactions associated with acetaminophen. It is difficult to determine how frequently serious skin reactions occur with acetaminophen, due to the widespread use of the drug, differences in usage among individuals (e.g., occasional vs. long-term use), and the long period of time that the drug has been on the market; however it is likely that these events occur rarely.

FDA will require that a warning be added to the labels of prescription drug products containing acetaminophen to address the risk of serious skin reactions. FDA will also request that manufacturers add a warning about serious skin reactions to the product labels of over-the-counter (OTC) acetaminophen drug products marketed under a new drug application. Healthcare professionals should be aware of this rare risk and consider acetaminophen when assessing patients with potentially drug-induced skin reactions.

In Hong Kong, there are 929 registered pharmaceutical products containing paracetamol, which is named acetaminophen in the US. DH had not received any adverse drug reaction report in relation to paracetamol. In view of FDA's recommendations, a letter to healthcare professionals was issued on 2 August 2013, and 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 decided at its meeting in September that DH should keep vigilant on the issue and actions taken by other regulatory authorities for future consideration when necessary.

The Mainland: Injectable levofloxacin may be associated with severe hypersensitivity reactions

On 2 August 2013, the China Food and Drug Administration (CFDA) alerted on the risk of severe hypersensitivity reactions associated with injectable levofloxacin. In the year 2012, the National Centre for Adverse Drug Reaction (ADR) Monitoring of China received 1,431 cases of ADRs related to injectable levofloxacin. The top three ADRs were anaphylactic shock, and events associated with skin and respiratory systems. They accounted for 60.24% cases. After the analysis of the case reports, the CFDA recommended:

1. healthcare professionals are reminded that the appropriate route of administration should be given to patients, as the bioavailability of levofloxacin is high and well absorbed after oral administration. Those who can be administered by oral route are not recommended to use injection;

2. when injectable levofloxacin is used, healthcare professionals should pay attention to the dosage regime, special populations, to avoid off-label use and the contraindications. In addition, injectable levofloxacin should be used with caution in patients with history of hypersensitive and allergy to quinolones, as well as patients with epilepsy or other central nervous system diseases. Levofloxacin injection should not be co-administered with any medicines in order to avoid any drug interactions, and the concomitant use with alkaline liquids, cephalosporins or injectable Chinese medicines should be avoided; and

3. the pharmaceutical manufacturers are advised to revise the product inserts, to strengthen the post-marketing ADR monitoring and actively carry out quality and technology research. Meanwhile, they should also protect the public health safety by means of promoting the safe use of the medicine via training and rational drug use.

In Hong Kong, three injectable levofloxacin products are registered. They are prescription only medicines indicated for the treatment of adults with bacterial infections. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

Singapore / Canada: Risk of Rat Sarcoma Viral Oncogene (RAS)-mutant malignancy progression and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS Syndrome) associated with Zelboraf® (vemurafenib)

It was noted from HSA website on 7 August 2013 that Roche in Singapore informed healthcare professionals of the risk of Rat Sarcoma Viral Oncogene (RAS)-mutant malignancy progression and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome associated with Zelboraf® (vemurafenib). The risk of RAS-mutant malignancy progression is based on a single report from a literature article about a 76 year-old male patient with stage IV melanoma in whom accelerated growth of a pre-existing neuroblastoma RAS-mutated chronic myelomonocytic leukemia was observed shortly after initiation of treatment with Zelboraf®. Based on its mechanism of action, Zelboraf® may cause progression of cancers associated with RAS mutations. Zelboraf® should be used with caution in patients with prior or concurrent cancers associated with RAS mutations. In addition, cases of DRESS syndrome have been reported with the use of Zelboraf® with onset ranging from 7 to 25 days. Zelboraf® treatment should be permanently discontinued if a patient develops DRESS syndrome. The local package insert will be updated to reflect the new safety information.

On 20 August 2013, similar letter was also issued by the local agency of Roche in Canada and was reported in its website. The local package insert of

Zelboraf® will be updated to reflect the new recommendations.

In Hong Kong, there is one vemurafenib-containing pharmaceutical product registered, namely Zelboraf Film-coated Tab 240mg (HK-61970). It is a prescription only medicine registered by Roche and is indicated in monotherapy for the treatment of adults with BRAF V600 mutation-positive unresectable or metastatic melanoma. Roche issued a Direct Healthcare Professional Communication about this on 24 July 2013. The current insert of the product has included the warning on the relevant safety information. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any action deemed necessary.

Macau: Recall of Kemudin (ceftriaxone) IM Injection 1g/3.5ml and Kemudin (ceftriaxone) IV Injection 1g/10ml

On 5 August 2013, the Health Bureau of Macau (HBM) announced that National Authority of Medicines and Health Products (INFARMED) of Portugal reported deficiencies were found in the manufacturing process at "Medreich Ltd. – Unit V" in India, which is the contract manufacturer of "Basi Lab.–Pharmaceutical S.A." in Portugal. As a result, seven products were recalled in Portugal. Out of these products, only two, namely Kemudin (ceftriaxone) IM Injection 1g/3.5ml and Kemudin (ceftriaxone) IV Injection 1g/10ml, have been imported into Macau. In order to protect the health of the public, HBM instructed importers and wholesalers to recall the products concerned. The medical institutions and clinics must also stop the drugs administered to the patient, and use other medicines as alternative sources.

In Hong Kong, the seven recalled products in Portugal are not registered pharmaceutical products. However, there are five registered pharmaceutical products which are manufactured by Medreich Ltd. – Unit V in India. They are Zoxon for Inj 1g (HK-56653), Axacef Tab 250mg (HK-57855), Axacef Tab 500mg (HK-56091), Axacef 125 Granules for Oral Suspension 125mg/5ml (HK-62036) and Zafalex 500 Cap 500mg (HK-60562). All are registered by Medreich Far East Ltd. (Medreich) and are prescription only medicines. According to Medreich, Zoxon for Inj 1g, Axacef Tab 250mg and 500mg have been imported into Hong Kong. Samples of the above three products were collected from Medreich and were analysed by the Government laboratory with no irregularities found. DH had not received any adverse drug reaction report in connection with the products, and will keep vigilant against any updated safety news on the issue. DH has instructed Medreich to temporary withhold the sale of these products. DH investigation continues.

US: Label changes on the risk of possibly permanent nerve damage from fluoroquinolones taken by mouth or by injection

On 15 August 2013, FDA required the drug labels and Medication Guides for all fluoroquinolones be updated to better describe the serious side effect of peripheral neuropathy. This serious nerve damage potentially caused by fluoroquinolones may occur soon after these drugs are taken and may be permanent. The risk of peripheral neuropathy occurs only with fluoroquinolones that are taken by mouth or by injection. Peripheral neuropathy is an identified risk of fluoroquinolones and was added to the Warnings or Warnings and Precautions sections of all the US labels for systemic (oral and injectable) fluoroquinolone drugs in 2004. The risk of peripheral neuropathy is also described in the Medication Guides for these products.

FDA has continued to receive reports of peripheral neuropathy even after the adverse reaction was added to the fluoroquinolone drug labels. The results of FDA's recent review of the Adverse Event Reporting System database indicate that although the risk of peripheral neuropathy is described in the drug labels of each marketed systemic fluoroquinolone, the potential rapid onset and risk of permanence were not adequately described. If the patient develops symptoms of peripheral neuropathy, the fluoroquinolone should be stopped and an alternative non-fluoroquinolone antibacterial drug should be used, unless the benefit of continued treatment with a fluoroquinolone outweighs the risk.

Safety Update

In Hong Kong, there are 199 registered pharmaceutical products containing fluoroquinolones in oral or injectable forms. They are prescription only medicines indicated for the treatment of adults with various bacterial infections such as infections of the respiratory tract, skin and urinary tract. DH had not received any adverse drug reaction report in relation to fluoroquinolones. In view of FDA's latest recommendation, a letter to healthcare professionals was issued on 16 August 2013, and the matter will be discussed in the meeting of the Registration Committee.

US: Investigating rare brain infection with the use of Gilenya (fingolimod)

On 29 August 2013, FDA alerted the public that a patient in Europe diagnosed with possible multiple sclerosis (MS) after taking the drug Gilenya (fingolimod). This is the first case of progressive multifocal leukoencephalopathy (PML), reported following the administration of Gilenya to a patient who had not previously received Tysabri (natalizumab), an MS drug associated with a higher risk of PML. PML is a rare and serious brain infection caused by the John Cunningham virus that damages the fatty covering of the brain called myelin. PML usually causes death or severe disability. Gilenya is used to treat relapsing forms of MS, a nervous system disease that affects the brain and spinal cord. Novartis reports that approximately 71,000 patients worldwide have been treated with Gilenya. Gilenya's manufacturer, Novartis, is currently investigating the PML case by reviewing all available information about this occurrence. FDA will communicate its final conclusions and recommendations after the evaluation is complete.

In Hong Kong, Gilenya Hard Capsules 0.5mg (HK-61192) is a prescription only medicine registered by Novartis Pharmaceuticals (HK) Ltd. and is indicated for multiple sclerosis. DH had not received any adverse event report in connection with the use of the product. DH will keep vigilant on any safety updates of the drug and actions taken by overseas regulatory authorities for consideration of any further action deemed necessary.

Drug Recall

Batch recall of Apo-Gliclazide Tablet 80mg (HK-51025)

On 1 August 2013, DH endorsed a licensed drug wholesaler, Hind Wing Co. Ltd. (Hind Wing), to recall from shelves one batch of Apo-Gliclazide Tablet 80mg (batch number: KE9991) due to a potential quality issue. Apo-Gliclazide Tablet 80mg, containing gliclazide, is a prescription only medicine used for the treatment of diabetes. It can only be supplied by pharmacies under the supervision of a registered pharmacist upon doctors' prescription.

DH received notification from Hind Wing that the product's manufacturer in Canada, Apotex Inc., found some batches of the product that might have come into contact with a cotton cleaning wipe during the production process. Apotex Inc. thus initiated a recall of the affected batches as a precautionary measure.

According to Hind Wing, only one of the affected batches (batch number: KE9991) had been imported to Hong Kong since October 2012. About 500 bottles (100 tablets each) were supplied to local dispensaries, private doctors and a private hospital. The rest were exported to Macau. DH had already informed the relevant authority of Macau on details of the recall. DH had closely monitored the recall. As of 1 August 2013, DH had not received any adverse reaction report related to the use of the product. A press statement was released on the same day to alert the public of the recall.

Members of the public who are in doubt should seek advice from their healthcare providers.

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.

Useful Contact

Drug Complaint:

Tel: 2572 2068
Fax: 3904 1224
E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

Tel: 2319 2920
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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.