Drug News
藥 物 情 報

Issue Number 47

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

Canada: Association of Sutent (sunitinib malate) with Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

On 6 September 2013, Pfizer Canada Inc., in collaboration with Health Canada, announced an important revision to the Product Monograph for Sutent (sunitinib malate). A statement was added about a potential association between the use of Sutent and severe cutaneous reactions suggestive of Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). Cases of SJS and TEN, including fatal cases, have been very rarely reported in patients who have used Sutent. Health Canada advised healthcare professionals that if signs or symptoms of SJS or TEN are present, Sutent treatment should be discontinued; and if the diagnosis of SJS or TEN is confirmed, treatment must not be restarted.

This potential risk of the cutaneous adverse events of SJS and TEN with sunitinib use was evaluated using a review of currently available safety data from published literature. Out of an estimated 214,848 patients exposed to sunitinib between 26 January 2006 and 30 April 2013, there were 5 reported cases of SJS and 4 reported cases of TEN internationally, although diagnosis was not confirmed in all cases. Two of the potential TEN cases had fatal outcomes.

In Hong Kong, there are four registered pharmaceutical products containing sunitinib malate, namely Sutent Cap 12.5mg (HK-55406), Sutent Cap 25mg (HK-55404), Sutent Cap 50mg (HK-55405) and Sutent Cap 37.5mg (HK-59785). All are registered by Pfizer Corporation HK Ltd. They are prescription only medicines indicated for the treatment of various tumours such as gastrointestinal stromal tumour, advanced renal cell carcinoma and pancreatic neuroendocrine tumours. In view of Health Canada's recommendation, a letter to healthcare professionals was issued on 9 September 2013, 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.

US: Labelling changes and postmarket study requirements for extended-release and long-acting opioid analgesics

On 10 September 2013, the Food and Drug Administration (FDA) of the United States (US) announced class-wide safety labelling changes and new postmarket study requirements for all extended-release and long-acting (ER/LA) opioid analgesics intended to treat pain. The updated indication stated that ER/LA opioids are indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The label should retain that the drugs are not intended for use as an "as-needed" pain reliever. Furthermore, it should say that: "Because of the risks of addiction, abuse and misuse, even at recommended doses, and because of the greater risks of overdose and death with these drugs, these drugs should be reserved for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain." Recognizing that more information is needed to assess the serious risks associated with long-term use of ER/LA opioids, FDA is requiring the manufacturers to conduct

further studies and clinical trials, to study certain known serious risks when these drugs are used long -term.

FDA is also requiring a new boxed warning on ER/ LA opioid analgesics to caution that chronic maternal use of these products during pregnancy can result in neonatal opioid withdrawal syndrome (NOWS), which may be life-threatening and require management according to protocols developed by neonatology experts. NOWS can occur in a newborn exposed to opioid drugs while in the mother's womb. Symptoms may include poor feeding, rapid breathing, trembling, and excessive or high-pitched crying.

In Hong Kong, there are 24 pharmaceutical products belong to ER/LA opioid analgesics, including the following ingredients: hydromorphone, morphine, oxycodone, tramadol, buprenorphine and fentanyl. They are prescription only medicines indicated for use as analgesics. In view of the FDA's recommendation, a letter to healthcare professionals was issued on 11 September 2013, and the matter will be discussed in the meeting of the Registration Committee.

US: Packaging changes to minimize risk of accidental exposure for Duragesic (fentanyl) Patches

Subsequent to the announcement by FDA in April 2012 to remind the public and healthcare professionals about the appropriate storage, use and disposal of fentanyl patches so as to prevent potential life-threatening harm from accidental exposure, FDA further announced the requirement on the color changes to the writing on Duragesic (fentanyl) pain patches on 23 September 2013. Patients and healthcare professionals are also reminded that fentanyl patches are dangerous even after they have been used because they still contain high amounts of strong narcotic pain medicine. Accidental exposure to these patches can cause serious harm and death in children, pets, and others.

In an effort to minimize the risk of accidental exposure to fentanyl patches, FDA is requiring the manufacturer of Duragesic to print the name and strength of the drug on the patch in long-lasting ink, in a colour that is clearly visible to patients and caregivers. The current ink colour varies by strength and is not always easy to see. This change is intended to enable patients and caregivers to more easily find patches on patients' bodies and see patches that have fallen off, which children or pets could accidentally touch or ingest. Used fentanyl patches require proper disposal after use - fold the patch, sticky sides together, and flush it down the toilet right away. The manufacturers of generic fentanyl patches are being requested to make similar changes.

In Hong Kong, there are six fentanyl-containing patches registered and all are prescription only medicines. They are opioid analgesics indicated for the management of chronic and intractable pain. The issue was reported in Drug News Issue No. 30 and a letter to healthcare professionals was issued on 20 April 2012. The Department of Health (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.

Australia: Apixaban (Eliquis), dabigatran (Pradaxa) and rivaroxaban (Xarelto) - risk factors for bleeding

On 24 September 2013, Therapeutics Goods Administration (TGA) announced that the oral anticoagulants apixaban (Eliquis), dabigatran (Pradaxa) and rivaroxaban (Xarelto) are now funded by the Pharmaceutical Benefits Scheme (PBS). As use of these medicines is likely to increase following the recent changes to their PBS listing, it is timely to remind health professionals of the need to carefully consider each patient's risk factors for bleeding and observe the dosage recommendations, contraindications and precautions for use outlined in the respective Product Information (PI) when prescribing these oral anticoagulants. Clinical trials and post-marketing experience have shown that major bleeding events, including those leading to death, have occurred with all of these products and with other anticoagulants. At this time, there is no specific antidote available for these medicines, and there are no current recommendations for the routine monitoring of anticoagulant activity once they are administered.

Prescribers should consider the following when prescribing these oral anticoagulants:

- patients should have renal function measured before commencing therapy;

- all should be used with caution in patients with an increased bleeding risk;
- a patient's bleeding risk increases with age;
- bleeding risk is increased with concomitant use of aspirin, clopidogrel and non-steroidal anti-inflammatory drugs. Each of these oral anticoagulants has additional drug-drug interactions that need to be taken into account;
- during regular patient follow up, check for evidence of bleeding and monitor renal function; and
- patients should be informed of the signs and symptoms of bleeding and the need to seek medical attention immediately if bleeding is suspected.

In Hong Kong, there are two registered pharmaceutical products containing apixaban, namely Eliquis Tab 2.5mg (HK-61377) and Eliquis Tab 5mg (HK-62094); three containing dabigatran, namely Pradaxa Cap 75mg (HK-57316), Pradaxa Cap 110mg (HK-57315) and Pradaxa Cap 150mg (HK-60516); and three containing rivaroxaban, namely Xarelto Tab 10mg (HK-57861), Xarelto Tab 15mg (HK-61396) and Xarelto Tab 20mg (HK -61395). All of them are prescription only medicines indicated for the prevention of stroke and systemic embolism in adult patients. Safety alerts on Pradaxa had been released by various overseas regulatory authorities which had been reported in previous Drug News. The decision made by the Registration Committee regarding the risk of bleeding with the use of Pradaxa was reported in Drug News Issue No. 37. The Registration Committee decided that the warning on the sales pack or package insert of dabigatran-containing products should be strengthened to include its contraindicated use in patients with lesion or condition at significant risk of major bleeding, such as current or recent gastrointestinal ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms or major intraspinal or intracerebral vascular abnormalities. In view of the TGA's safety advisory for doctors when prescribing these oral anticoagulants, a letter to inform healthcare professionals was issued on 25 September 2013. 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.

UK: No evidence that cervical cancer vaccine Cervarix causes chronic fatigue syndrome

On 26 September 2013, the Medicines and Healthcare products Regulatory Agency (MHRA) of United Kingdom (UK) announced that it has found no evidence that Cervarix – the human papillomavirus (HPV) vaccine – may cause chronic fatigue syndrome. Cervarix was given to over two million young women aged between 12 and 18 years as part of the Government's HPV vaccination programme in the UK between September 2008 and September 2012. The MHRA's scientists conducted their study after reports that some women were suffering from chronic fatigue syndrome following vaccination. Scientists at the MHRA analysed patient record data from the Clinical Practice Research Datalink (CPRD) to compare the frequency of fatigue syndromes in young women before and after the start of the vaccination programme and the risk following vaccination compared to other time periods. The study, published in the journal Vaccine, found no evidence of an increased risk of chronic fatigue syndrome in women after having the Cervarix vaccine. This conclusion supports earlier reporting trends from the MHRA's Yellow Card surveillance system.

In Hong Kong, Cervarix Vaccine (Pre-filled Syringe) (HK-56180) is registered by GlaxoSmithKline Ltd. and it is a prescription only medicine. It is used in the prevention of premalignant cervical lesions and cervical cancer in females ≥9 years causally related to certain oncogenic HPV types. DH will keep vigilant on new safety updates of the vaccine.

US: Tygacil (tigecycline) may be associated with increased risk of death

On 27 September 2013, FDA notified health professionals and their medical care organizations of a new Boxed Warning describing an increased risk of death when intravenous Tygacil is used for FDA-approved uses as well as for non-approved uses. These changes to the Tygacil Prescribing

Safety Update

Information are based on an additional analysis that was conducted for FDA-approved uses after FDA issued a Drug Safety Communication about this safety concern in September 2010.

This analysis showed a higher risk of death among patients receiving Tygacil compared to other antibacterial drugs: 2.5% (66/2640) vs. 1.8% (48/2628), respectively. The adjusted risk difference for death was 0.6% with corresponding 95% confidence interval (0.0%, 1.2%). In general, the deaths resulted from worsening infections, complications of infection, or other underlying medical conditions.

Tygacil is FDA-approved to treat complicated skin and skin structure infections, complicated intra-abdominal infections, and community-acquired bacterial pneumonia. Tygacil is not indicated for treatment of diabetic foot infection or for hospital-acquired or ventilator-associated pneumonia. Healthcare professionals should reserve Tygacil for use in situations when alternative treatments are not suitable. Patients and their caregivers should talk with their healthcare professionals if they have any questions or concerns about Tygacil.

In Hong Kong, there is one registered pharmaceutical product containing tigecycline, namely Tygacil for Injection 50mg (HK-54821). It is a prescription only medicine indicated for the treatment of complicated skin and skin structure infections, complicated intra-abdominal infections and community-acquired bacterial pneumonia. The increased mortality risk had been released by FDA and the European Medicines Agency (EMA) which had been reported in Drug News Issues No. 11 and No. 17. The Registration Committee then decided that the sales pack label and/or package insert should state that the medicine should only be used in its approved therapeutic indications and only when other antibiotics are not suitable. In view of FDA's latest announcement, a letter to inform healthcare professionals was issued on 30 September 2013, and the matter will be discussed in the meeting of the Registration Committee.

Drug Recall

Suspension of supply and use of one batch of Xolair for Injection with Solvent 150mg (HK -54330)

On 18 September 2013, DH requested a licensed drug wholesaler, Novartis Pharmaceuticals (HK) Ltd. (Novartis), to suspend the supply and use of a batch (S1700) of Xolair for Injection with Solvent 150mg, due to quality issue. Xolair is a presciption only medicine used for control of asthma.

Novartis reported to DH that the manufacturer of the product in Switzerland identified a manufacturing deviation which caused the introduction of silicone into some batches of the product. According to Novartis, no complaint related to the quality issue was received.

According to Novartis, 60 packs of one of the affected batches (S1700) had been imported into Hong Kong in early August 2013 and some were supplied to Hospital Authority, private hospitals and private doctors. According to the preliminary investigation of Novartis, the quality issue might not pose undue risk to patients. However, as a precautionary measure, Novartis suspended further supply of the batch, and issued a letter to alert the affected hospitals and doctors about the issue. DH had not received any adverse reaction report related to the product.

DH has required Novartis to provide detail investigation report and will keep vigilant of the latest situation of the issue.

Public urged not to use cosmetic product with undeclared Western drug ingredient

On 13 September 2013, DH urged members of the public not to use a cosmetic product labelled as "Alive Skin" as it was found to contain an undeclared western drug ingredient.

Upon the investigation of a public complaint, the DH found that the above product was being offered for sale by a beauty centre in Tsim Sha Tsui. Analysis conducted by the Government Laboratory revealed that the product contained an undeclared Part I poison, namely clobetasol propionate.

The beauty centre was raided during a joint operation by the DH and the Police. During the operation, a 54-year-old woman was arrested for suspected illegal sale of an unregistered pharmaceutical product and Part I poison.

Clobetasol propionate is a corticosteroid used for the topical treatment of severe inflammatory skin disorders and is a prescription medicine to be used under medical advice. Inappropriate use of corticosteroids may cause serious side-effects such as Cushing's syndrome with symptoms including moon face and muscle atrophy.

A press statement was released on the same day to alert the public of the incident.

Man arrested for illegal sale of unregistered pharmaceutical product with suspected controlled Western drug ingredients

On 24 September 2013, a joint operation was conducted by DH and the Police resulting in the arrest of a 37-year-old man for illegal sale of two unregistered pharmaceutical products, namely Finpecia tablets and Kirkland Signature Minoxidil Topical Solution, with suspected controlled western drug ingredients.

Upon the investigation of a public complaint, DH found that the above two products were being offered for sale on the Internet. The products were labelled as containing finasteride and minoxidil respectively. Both are Part I poisons, while finasteride is also a prescription only drug. Hong Kong pharmaceutical product registration numbers were not found on any of the product labels.

Finasteride is generally used for the treatment of hair loss, with side-effects including decreased libido and erectile dysfunction. Minoxidil is commonly used topically for the treatment of hair loss, with side-effects including scalp irritation and itchiness.

A press statement was released on the same day to alert the public of the 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 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.

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.