Drug News
藥 物 情 報

Issue No. 36 : October 2012

This is a monthly digest of local and overseas drug safety news and information released by the Drug Office of the Department of Health in the month as stated above. 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: Risk of atypical fracture with Prolia® (denosumab)

On 5 October 2012, Health Sciences Authority (HSA) of Singapore notified healthcare professionals of the risk of atypical femoral fracture with Prolia®. During the ongoing open-label extension study of the pivotal phase 3 fracture trial in postmenopausal osteoporosis (FREEDOM), cases of atypical femoral fracture had been confirmed in patients receiving Prolia®. These events had occurred very rarely (<1/10,000) based on 31,266 subject-years exposed to Prolia® in bone loss studies. The Prolia® package insert in Singapore had been updated with atypical femoral fracture as a new warning and as an adverse drug reaction.

In Hong Kong, Prolia Solution for Injection in Pre-filled Syringe 60mg/ml (USA) (HK-60588) and Prolia Solution for Injection in Pre-filled Syringe 60mg/ml (The Netherlands) (HK-60589) are prescription medicines registered by GlaxoSmithKline Ltd. Prolia is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture. The application of inclusion of the risk of atypical femoral fracture in the product insert has been submitted and approved.

EU: European Medicines Agency finalised review of recent published data on cardiovascular safety of NSAIDs

Following an alert issued by the European Medicines Agency (EMA) in October 2011 about the cardiovascular safety of non-steroidal anti-inflammatory drugs (NSAIDs), EMA had finalised the review of recently published information and released the news on 19 October 2012. The Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that evidence from newly available published data confirmed findings from previous reviews conducted in 2005 and 2006: there were no new safety concerns regarding cardiovascular and gastrointestinal safety and serious skin reactions with non-selective NSAIDs, and the benefit-risk balance remained favourable. The CHMP was of the opinion that the current treatment advice for naproxen and ibuprofen had adequately reflected their safety and efficacy. As compared with other NSAIDs, a consistent but small increase in the risk of cardiovascular side effects was seen for diclofenac which was comparable to the risk seen with selective COX-2 inhibitors. As a follow-on to this review, the Agency's new Pharmacovigilance Risk Assessment Committee (PRAC) would assess all available data on diclofenac (both published and unpublished) to consider the need for updating the treatment advice.

In Hong Kong, NSAIDs-containing products are registered pharmaceutical products with ingredients such as diclofenac, ibuprofen, naproxen, indomethacin, mefenamic acid and piroxicam. They are indicated for the treatment of arthritis and many other painful conditions, including headache, fever, and minor ailments. The cardiovascular risk of NSAIDs has been reported in Issue No. 24 of Drug News and a letter to healthcare professionals was issued on 30 September 2011. 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.

Canada: Label update on the interaction of Proton Pump Inhibitors with Methotrexate

On 19 October 2012, Health Canada informed healthcare professionals regarding the update of the labelling for Proton Pump Inhibitors (PPIs) and methotrexate to include information on a potential interaction between these products. The use of these products concurrently by patients may increase serum methotrexate level, which could lead to side effects. The possible health risks include kidney failure, low red blood cell count, inflammation of the digestive tract, irregular heartbeat, muscle pain, infections, and diarrhea. While a definite association between PPIs use and an increase in methotrexate had not been confirmed, there had been a number of studies suggesting a possible interaction between PPIs and methotrexate. The potential for an increased risk of methotrexate side effects was very likely, which was the reason of Health Canada to announce this change in labelling.

In Hong Kong, there are 145 proton pump inhibitors registered. The ingredients include esomeprazole, lansoprazole, dexlansoprazole, omeprazole, pantoprazole and rabeprazole. All these products are prescription medicines except the products containing omeprazole. They are used as antacids, antireflux and antiulcerants. For products containing methotrexate, there are 16 registered products and all are prescription medicines. They are indicated for the treatment of malignant tumours and autoimmune diseases. In view of Health Canada's recommendation, a letter to healthcare professionals was issued on 22 October 2012, and the matter will be discussed in the meeting of the Registration Committee of the Pharmacy and Poisons Board.

UK: Alert on all medical devices and medicinal products containing chlorhexidine

On 25 October 2012, the Medicines and Healthcare Products Regulatory Agency (MHRA) of UK alerted the risk of anaphylactic reaction for all medical devices and medicinal products containing chlorhexidine. MHRA had received a number of reports of anaphylactic reactions following the use of products containing chlorhexidine and there were also other reports of allergic reactions to chlorhexidine published in journals. MHRA advised that healthcare professionals should be aware of the potential anaphylactic reaction of chlorhexidine and ensure that known allergies were recorded in patient notes; and should check the products' labels and instructions for use prior to use on patients with a known allergy of products contained chlorhexidine.

In Hong Kong, there are 92 registered pharmaceutical products containing the antiseptic chlorhexidine. Drug Office had not received any adverse event report in connection with the use of chlorhexidine. In view of the MHRA's alert, a letter to inform healthcare professionals was issued on 26 October 2012, and the matter will be discussed in the meeting of Registration Committee of the Pharmacy and Poisons Board.

US: Serious adverse events from accidental ingestion by children of some over-the-counter eye drops and nasal sprays

On 25 October 2012, the Food and Drug Administration (FDA) of US warned healthcare professionals and the public about the accidental ingestion by children of over-the-counter eye drops could result in serious and life-threatening adverse events. The cases of accidental ingestion involving active ingredients tetrahydrozoline, oxymetazoline or naphazoline, which are used to relieve redness and nasal congestion, occurred in children 5 years of age and younger had been reviewed by FDA. No deaths were reported, though serious events requiring hospitalization such as tachycardia, decreased respiration, hypertension, sedation, somnolence, mydriasis, stupor, hypothermia, and coma had occurred. Ingestion of small amount (1-2 mL) of these products could lead to serious adverse events in young children. As most of these redness-relief eye drops and nasal decongestant sprays are not packaged with child-resistant closures, children could accidentally ingest the drug if the bottles were within easy reach. FDA advised that consumers should always store these products at places out of the reach of children.

In Hong Kong, there are 97 registered over-the-counter pharmaceutical products containing ingredients for relieving eye redness and nasal congestion: tetrahydrozoline, oxymetazoline or naphazoline. Drug Office had not received any adverse event report in connection with the use of products containing these ingredients, and will keep

vigilant against any updated safety news related to the issue.

EU / Canada / UK: Update on seasonal influenza vaccines produced by Novartis Vaccines in Italy

On 26 October 2012, EMA announced that a number of European Union (EU) Member States had halted the use, as a precautionary measure, of some anti-influenza vaccines manufactured by Novartis Vaccines, because of a suspected quality defect. It involved the aggregation of proteins which were predominantly influenza virus-derived (mainly haemagglutinin). The Italian Medicines Agency (AIFA) was first informed of the suspected quality defect by the manufacturer (Novartis Vaccines) located in Italy. AIFA took the lead on behalf of the EU in investigating the suspected quality defect in order to determine whether it affected the safety and efficacy of these vaccines, and whether the affected batches should be permanently removed from the market. EMA and the Member States continued to monitor the situation.

In response to this recommendation released by EMA, on 26 October 2012, Health Canada asked Novartis to suspend distribution of the seasonal flu vaccines Agriflu and Fluad until a full review of the situation was completed. On 31 October 2012, Health Canada had completed the review and released the vaccines for immediate use.

On 30 October 2012, MHRA also announced the recall of two batches of Agrippal suspension for injection in pre-filled syringe (lot numbers: 126201A and 126102) due to the same reason as stated above. Agrippal suspension for injection is the influenza vaccine marketed by Novartis Vaccines and Diagnostics S.r.l.

In Hong Kong, Agriflu is not a registered pharmaceutical product, whereas Agrippal S1 Vaccine Pre-filled Syringe Injection (Agrippal) (HK -50901) and Fluad Vaccine Pre-filled Syringe Injection (Fluad) (HK-50982) are influenza vaccines manufactured by Novartis Vaccines and Diagnostics S.R.L., Italy. Both are prescription medicines registered by Novartis Pharmaceuticals (Novartis) (HK) Ltd.. On 25 October 2012, the Department of Health (DH) was informed by Novartis that Agrippal and Fluad were suspended in Italy and Switzerland due to the aggregation of proteins in the vaccines. According to Novartis, Agrippal was not available in Hong Kong as the last imported batch had already been expired in May 2012, and Fluad had never been marketed in Hong Kong. On 13 November 2012, Novartis informed DH that the suspension of Agrippal and Fluad by AIFA had been lifted. After investigation, AIFA reaffirmed the safety and efficacy of the vaccines. Moreover, Health Canada and Swissmedic had also lifted the suspension of the products in Canada and Switzerland respectively.

UK: Hypotonic saline solution: do not use in children except in specialist settings under expert supervision

On 30 October 2012, MHRA reported that a review of the risks and benefits of 0.18% saline/4% glucose solution (hypotonic saline) when used in children was recently undertaken by the MHRA and the Commission on Human Medicines (CHM). The review followed an inquiry into the deaths of three children in the UK who died from cerebral oedema caused by hyponatraemia after receiving intravenous hypotonic saline. On the basis of the review, the CHM recommended that such solution should not be used in children aged 16 years or less, except under expert medical supervision in paediatric specialist settings such as kidney, heart, liver, high-dependency and intensive care units.

In Hong Kong, there are four registered injectable pharmaceutical products containing 0.18% saline, namely 0.18% Sodium Chloride and 4.3% Dextrose Injection (HK-12411), 0.18% Sodium Chloride and 4.3% Glucose Injection (HK-28206), 0.18% Sodium Chloride and 4.3% Dextrose Injection (Thai Otsuka) (HK-55595) and 0.18% Sodium Chloride and 4.3% Glucose Intravenous Infusion (PT Otsuka) (HK-56868). These products are indicated for the maintenance and replacement of body fluid. In view of MHRA's recommendation, a letter to healthcare professionals was issued on 30 October 2012. Healthcare professionals were advised to balance the benefit against the risk of possible adverse effects related to the use of hypotonic saline. Moreover, healthcare professionals should be aware and promptly recognize signs and symptoms of hyponatraemia (headache, nausea, seizures, lethargy, coma cerebral oedema) in children receiving hypotonic intravenous fluids.

Total recall of Inflexal V Injection (HK-50625)

On 4 October 2012, DH endorsed a licensed drug wholesaler, Amedis Co. Ltd. (Amedis), to conduct a total recall of Inflexal V Injection - 2012/2013 seasonal influenza vaccine (Inflexal) from market because of quality issue. It is a prescription medicine which can only be sold with doctor's prescription and under the supervision of pharmacists at registered pharmacies.

The recall was initiated because product's Swiss manufacturer, Crucell Switzerland AG (Crucell), found that two batches of the product in the manufacturing site were found contaminated with bacteria.

According to information available so far, only two batches of Inflexal (lot numbers: 3000287.03 and 3000291.02) had been imported into Hong Kong and the risk of contamination of these two batches were remote. These two batches were manufactured in August which was different from those affected batches in Switzerland. Their certificates of analysis showed that the imported vaccines had passed all quality tests, including sterility testings.

To meet the high demand of influenza vaccines in the flu season, Swissmedic allows the influenza vaccines to be released to wholesalers pending the release certificates been issued. However, the vaccines can only be distributed to the market after the Swissmedic has officially signed the release certificates. For this incident, a total of 21,071 boxes containing single injection of Inflexal and 2,211 boxes containing 10 injections of Inflexal were imported to Hong Kong in mid-September, pending notification from Crucell that the official release certificates had been issued. DH found that 3,179 boxes of single injection and 1,737 boxes of 10 injections had already been sold to about 300 private doctors before receiving such notification. DH contacted the Swissmedic subsequently and confirmed that the imported two batches had been certified to be released into the market on September 18, 2012 and on September 24, 2012 respectively. DH warned Amedis that notification of the official release certificate must be received before distribution of the product.

Based on the information available so far, it was considered that the potential risk of contamination of the two imported batches was remote. Nonetheless, DH considered the recall should be completed as scheduled according to international practice. DH had alerted the relevant parties about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports in connection with the product. A press statement was released on the same day to alert the public of the recall.

Batch recall of Panadol Cold & Flu Hot Remedy Powder - Lemon with Honey (HK-50932)

On 5 October 2012, DH endorsed a licensed drug wholesaler, GlaxoSmithKline Ltd. (GSK), to conduct a recall from market one batch of Panadol Cold & Flu Hot Remedy Powder - Lemon with Honey (Panadol) (lot number: 2004) as there were some packs of the product with wrongly printed expiry date on sachets. The product contains paracetamol, phenylephrine and vitamin C as ingredients and is an over-the-counter drug used to relieve cold and flu symptoms.

The printing mistake came to light following the enquiry received by GSK from a retailer. The correct expiry date for the affected batch of Panadol was 07-2014. It was printed correctly on the outer box but the expiry date of some sachets was wrongly printed as 07-2004.

According to GSK, 45,228 boxes of the affected batch were imported to Hong Kong on 14 September 2012 and 3,566 boxes were subsequently supplied to local pharmacies and medicine companies. DH had alerted the relevant parties about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports in connection with the product. A press statement was released on the same day to alert the public of the recall.

Total recall of six Rocephin Injections

On 11 October 2012, DH endorsed a licensed drug wholesaler, Roche HK Ltd. (Roche) , to conduct a total recall of six registered pharmaceutical products namely Rocephin for Inj 250mg IM (HK-20182) and IV (HK-52844), Rocephin for Inj 500mg IM (HK-20187) and IV (HK-20188), Rocephin for Inj 1g IM (HK-20192) and IV (HK-20190) from market because of stability issue. Rocephin Injections contain the antibiotic ceftriaxone and are prescription medicines.

The recall was initiated because the product's Swiss manufacturer, F. Hoffmann-La Roche Ltd, found that two batches of Rocephin for Inj 250mg IV (lot numbers: B1132 and B1133) were out of specification (OOS) for degradation product at the 30th month. The registered shelf life of the products was 36 months. According to the manufacturer, the OOS might be related to the suboptimal closure system of the injection vial.

Only one affected batch of Rocephin for Inj 250mg IV (lot number: B1132B01) had been imported to Hong Kong in February 2011. A total of 330 vials of this batch had been imported and they were all used. As a precautionary measure, Roche was conducting a total recall of all Rocephin Injections. The products had been supplied to the Hospital Authority (HA), private hospitals, private doctors and pharmacies and exported to Macau. DH had alerted the relevant parties about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports in connection with the products. A press statement was released on the same day to alert the public of the recall.

Members of the public were advised to consult their healthcare providers if they were in doubt or felt unwell after using the above products.

Batch recall of Nicorette Chewing Piece 4mg 105's (HK-25612)

On 19 October 2012, DH endorsed a licensed drug wholesaler, Johnson & Johnson Consumer (HK) Ltd. (J&J), to recall from market one batch of Nicorette Chewing Piece 4mg 105's (Nicorette) (lot number: NL752C) because of a labelling error. Nicorette contains nicotine and is an over-the-counter drug used for smoking cessation.

The mistake came to light following notification received from retailers. The promotional flag label of 2mg was wrongly affixed to the Nicorette 4mg batch by the local distributor Healthcare Division O/B LF Asia (HK) Ltd. (LF Asia). This labelling error might result in an increase in the occurrence of possible adverse effects, e.g. nausea, vomiting and headache, encountered by 2mg users who inadvertently used the 4mg gum.

According to J&J's, 614 boxes of the affected batch were imported to Hong Kong in December 2011 and the promotional flag label of 2mg was affixed to the outer box of the product by LF Asia. This batch was then released to the market in July 2012. A total of 461 boxes were supplied to the HA and retailers while 120 boxes were exported to Macau. DH had alerted the relevant parties about the matter and closely monitored the recall. So far, DH had not received any adverse drug reaction reports in connection with the product. A press statement was released on the same day to alert the public of the recall.

Labelling errors are an offence under the Public Health and Municipal Services Ordinance (Cap 132). The maximum penalty involved is a fine of $50,000 fine and six months' imprisonment.

Healthcare professionals and retailers must stop supplying, and customers must stop consuming, the said batch of the product immediately. For other batches, customers should check the product labelling before use. For those who have taken the affected product and are either in doubt or feeling unwell, they should consult their healthcare providers.

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: 3904 1224
E-mail: adr@dh.gov.hk
Link: http://www.drugoffice.gov.hk/adr.html
Post: ***Pharmacovigilance Unit,***
Drug Office, Department of Health,
Rm 1801, 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.