Drug News
藥 物 情 報

Issue No. 18 : April 2011

This is a monthly digest of local and overseas drug safety news and information released in the previous month. For the latest news and information, please refer to public announcements or the website of the Pharmaceutical Service of the Department of Health (http://www.psdh.gov.hk).

Safety Update

Canada: Recall of one lot of Ixiaro Japanese Encephalitis vaccine (inactivated, adsorbed)

17 March 2011 - Intercell AG and Novartis Pharmaceuticals Canada Inc. (Novartis), in consultation with Health Canada, recalled one lot of Ixiaro® (Japanese Encephalitis vaccine (inactivated, adsorbed) (lot number :JEV09L37C) because the potency tests at the 11-month stability time point for this lot suggested that, when administered after 23 December 2010, it might be less potent and not induce a full protective immune response in vaccinees. According to Novartis, there is no evidence of a safety concern and no other lots of Ixiaro were affected by this recall. Healthcare professionals were advised to stop using the sepcific lot and followed their patients who had been administered with the affected lot as suggested.

In Hong Kong, Ixiaro injection (Japanese encephalitis vaccine) is a prescription medicine registered by Novartis Pharmaceuticals (HK) Ltd. The company confirmed that the product has not been marketed in Hong Kong since it was registered.

UK: Updates on a drug alert of Lucentis 10mg/ml, 1x0.23ml

18 March 2011 – Following the alert about a potential problem with blocked Microlance 3 Becton -Dickinson injection needles in certain batches of administration packs of Lucentis in Febryary 2011, Novartis informed the MHRA of the UK that Lucentis administration packs incorporating unaffected injection needles, starting with batch S0052A and needle batch numbers 110211, was available and would be provided via the normal supply process.

In Hong Kong, Lucentis (ranibizumab) is a prescription medicine registered by Novartis Pharmaceuticals (HK) Ltd. Ranibizumab is a recombinant humanised monoclonal antibody used in the treatment of neovascular (wet) age-related macular degeneration. DH issued letters to advise healthcare professionals not to use injection needles supplied together with certain batches of Lucentis Injection packs on 15 February 2011. A press release was also announced on the same day. The company has imported new batches of Lucentis with unaffected injection needles since 14 March 2011.

US: Recall of alcohol prep pads made by the Triad Group in Forteo Starter Kits

21 March 2011 - Eli Lilly and Company announced that alcohol prep pads made by the Triad Group contained in the black starter kits for Forteo [teriparatide (rDNA origin) injection] in the United States should not be used due to potential contamination with the bacteria, Bacillus cereus, which could result in life threatening infections, especially in at-risk populations, including immune suppressed and surgical patients. According to the company, the starter kits that contained the Triad alcohol prep pads were black bags and were discontinued in June 2009. The bags are now blue and do not include Triad alcohol prep pads. Also, this recall did not affect or involve the Forteo Delivery Device.

In Hong Kong, Forteo pre-filled pen (teriparatide) is a prescription medicine registered by Eli Lilly Asia, Inc. Teriparatide is used for the treatment of osteoporosis. Alcohol prep pads have never been supplied with the registered package of the product in Hong Kong. Details about the recall of alcohol prep pads made by the Triad Group have been reported in Issue No. 16 of Drug News.

US: Updates on the safety review with the use of proton pump inhibitors

24 March 2011 - Subsequent to FDA's previous safety announcement released as reported in issue No. 8 of Drug News, the FDA considered an osteoporosis and fracture warning on the"Drug Facts" label of the over-the-counter (OTC) proton pump inhibitor (PPI) was not indicated at this time. On 25 May 2010, FDA notified the healthcare professionals and patients of revisions to the prescription and OTC labels for PPI to include new safety information about a possible increased risk of fractures of the hip, wrist, and spine with the use of these medications. Following a thorough review of available safety data, FDA concluded that fracture risk with short-term, low dose PPI use was unlikely. The available data showed that patients at highest risk for fractures received high doses of prescription PPIs (higher than OTC PPI doses) and/or used a PPI for one year or more.

In Hong Kong, there are 140 PPIs registered with the Pharmacy and Poisons Board (PPB). All are prescription medicines except omeprazole. PPIs work by reducing the amount of acid in the stomach and are used to treat conditions such as gastroesophageal reflux, stomach and small intestine ulcers, and inflammation of the esophagus. In response to the safety alert released by FDA in May last year, DH issued letters to healthcare professionals and a press release to inform the public about this issue on 26 May 2010. The safety information has also been reported in Issue No. 8 of Drug News.

Australia: Recall of vaccine Batch N3336 Pneumovax 23

25 March 2011 - The Therapeutic Goods Administration (TGA) of Australia announced an immediate recall of Batch N3336 of the vaccine Pneumovax 23 manufactured by Merck Sharp and Dohme (Australia) Pty Limited (MSD) as a precautionary measure following reports of a small number of adverse reactions in some patients who had received the vaccine. As of 24 March 2011, the TGA had received 10 reports of severe skin reactions with surrounding inflammation at the site of the vaccine injection. This batch of vaccine had only been supplied in New South Wales and the Australian Capital Territory and there was no indication of problems with any other batch of Pneumovax 23.

In Hong Kong, Pneumovax Vaccine (streptococcus pneumoniae) is a prescription pharmaceutical product registered by Merck Sharp & Dohme (Asia) Ltd and is used for immunisation against pneumococcal infection. The company confirmed that the recalled batch has not been imported into Hong Kong. DH has no record of untoward event report associated with Pneumovax. DH issued letters to inform healthcare professionals about the recall on 25 March 2011.

US: Special storage and handling requirements for Pradaxa capsules

29 March 2011 – US FDA alerted the public to the special storage and handling requirements for Pradaxa (dabigatran etexilate mesylate) capsules. Due to the potential for product breakdown from moisture and loss of potency, Pradaxa capsules should only be dispensed and stored in the original bottle or blister package. Healthcare professionals were advised to dispense Pradaxa capsules in the original manufacturer packaging. Patients were advised to store Pradaxa in the original bottle or blister package to protect from moisture instead of other container, such as pill boxes or pill organizers.

In Hong Kong, Pradaxa Cap 75mg and 110 mg are prescription medicines registered by Boehringer Ingelheim (HK) Ltd. It is used for primary prevention of venous thromboembolic events in adult patients. The company confirmed that only the blister package is registered and supplied in Hong Kong. The package insert contains information to remind patients to peel off the blister foil at time of use only.

UK: Updates on the recall of Dianeal, Extraneal and Nutrineal

6 April 2011 – Further to the previous recall of Baxter's peritoneal dialysis (PD) solutions in Europe as reported in Issue No. 15 and 16 of Drug News, the MHRA of UK annouced a recall of certain batches of Baxter's peritoneal dialysis (PD) solutions, namely Dianeal, Extraneal and Nutrineal. These products are sterile solutions used in patients who have to undergo peritoneal dialysis because of kidney failure. The recall was initiated because of potential presence of endotoxin in a some batches of

the PD solutions which may increase the risk of aseptic peritonitis. In fact, this was an ongoing issue and distribution of potentially affected stock had been allowed for several months due to the lack of acceptable alternative supplies throughout Europe. As new stock from alternative sources was available, the potentially affected stock was being recalled to minimise patient risk.

In Hong Kong, two Nutrineal products of Baxter Healthcare Ltd are registered, one is manufactured in Ireland (HK-45278) whereas the other is manufactured in Singapore (HK-51751). The company has confirmed that only the Nutrineal manufactured in Singapore is marketed in Hong Kong which is not on the recall list in the UK and Europe.

Singapore: Serious haematological reactions associated with quinine sulphate

6 April 2011 - HSA warned about the known complications of serious and life-threatening haematological reactions with quinine sulphate. Quinine sulphate is an antimalarial drug which is also used in some places for the treatmnet of nocturnal leg cramps. Healthcare professionals were advised not to use it for treating nocturnal leg cramps because of its unfavourable benefit-risk profile for this condition. As nocturnal leg cramps was not an approved indication of quinine sulphate in Singapore, HSA had requested the company to further strengthen the warnings on the package insert for quinine sulphate tablets.

In fact, several drug regulatory authorities, including the TGA of Australia and US FDA, had already required the removal of leg cramps from quinine-containing products' list of indications.

In Hong Kong, there are four registered pharmaceutical products containing quinine sulphate or quinine bisulphate and all of them are prescription medicines. DH has not received any adverse event report related to the products. In response, DH issued letters to the healthcare professionals and press release to inform public about this matter on 6 April 2011. They were also advised not to use pharmaceutical products containing quinine sulphate for the management of nocturnal leg cramps. Patients using these products were advised to consult healthcare professionals if in doubt or feel unwell. The issue was considered at the meeting of the Registration Committee of the Pharmacy and Poisons Board held on 11 May 2011. The Committee has decided to remove the approved indication of treating nocturnal leg cramps for products containing quinine and include treatment of nocturnal leg cramps as a contraindication on their sales pack label and/or package insert.

EU and UK: Withdrawal of marketing authorisation of Onsenal (celecoxib) in EU

In 2003, Onsenal (celecoxib) was marketed in the EU for the reduction of the number of adenomatous intestinal polyps in familial adenomatous polyposis (FAP), as an adjunct to surgery and further endoscopic surveillance. The European Commission (EC) issued a marketing authorisation of Onsenal under exceptional circumstances with specific obligation of the applicant, Pfizer Limited, to provide further data on its efficacy and safety.

In 2011, the CHMP of the EMA conducted the 8th annual reassessment of Onsenal and requested the applicant to provide supplementary information to confirm its benefits in treating FAP still outweigh its risks. On 10 March 2011, Pfizer Limited notified the EC its decision to voluntarily withdraw the marketing authorization for Onsenal because the company could not provide the additional data required, as a result of slow enrolment in an ongoing clinical trial. On 28 March 2011 the EC issued a decision to withdraw the marketing authorisation for Onsenal.

In Hong Kong, Onsenal Cap 400mg (HK53007) of Pfizer Corporation Hong Kong Ltd was a registered prescription medicine but it has never been marketed locally. The company also holds registration certificate of another celecoxib containing drug called Celebrex. Celebrex was indicated for osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, acute pain, primary dysmenorrheal and FAP. The package insert of Celebrex has been updated to delete the indication for FAP. DH issued letters to inform healthcare professionals about the latest information on 7 April 2011.

US: - Risk of methemoglobinemia associated with the use of topical products containing benzocaine

8 April 2011 – US FDA alerted healthcare

professionals and patients that the Agency continued to receive reports of methemoglobinemia, a serious and potentially fatal adverse effect, associated with benzocaine products in form of spray, gels and liquids sold over-the-counter. Benzocaine is a local anesthetic and is used to relieve pain from a variety of conditions, such as teething, canker sores, and irritation of the mouth and gums. Methemoglobinemia is a rare but serious and potentially fatal condition where there is a significant reduction in the amount of oxygen carried in the blood. It could occur with all strengths of benzocaine sprays, gels and liquids, and tended to affect mainly children aged two years or younger.

FDA recommended that these products should not be used on children less than two years of age, except under the advice and supervision of a healthcare professional. FDA is evaluating the safety of benzocaine products and pledges to update the public and take appropriate regulatory actions when necessary.

In Hong Kong, there are two pharmaceutical products containing benzocaine registered for topical oral use. Both products are part I poison and must be sold under the supervision of a pharmacist. One of them is approved for children 2 years of age and older and the other is approved for children over 3 years of age. So far, the DH has not received any relevant adverse event report. DH issued letters and a press statement to alert healthcare professionals and public respectively about this matter on 8 April 2011. The issue was considered at the meeting of the Registration Committee of the Pharmacy and Poisons Board held on 11 May 2011. It was decided that the sales pack label and/or the package insert of products containing benzocaine for topical oral use should state that they should not be used for children under 2 years of age and should also include a statement on the risk of methemoglobinemia associated with the use of these products. DH remains vigilant on the latest development worldwide.

US: Ongoing safety review of possible increased risk of developing new malignancies associated with Revlimid (lenalidomide)

9 April 2011 – US FDA informed the public that the Agency was reviewing all available new information on the potential risk of developing new malignancies with Revlimid (lenalidomide) as the results of several clinical trials found that patients treated with Revlimid might be at an increased risk of developing cancer, particularly acute myelogenous leukemia and B-cell lymphoma malignancy, compared to patients who did not take the drug.

At this time, FDA believed the benefits of Revlimid continued to outweigh the potential risks. FDA would communicate any new recommendations once it had completed its review.

In Hong Kong, the Revlimid Cap is registered as four different strengths, namely 5mg, 10mg, 15mg and 25mg. All these products are registered by Celgene Ltd and are prescription medicines. Revlimid is used in combination with dexamethasone for treating multiple myeloma patients who have received at least one prior therapy. DH issued letters to inform healthcare professionals about this matter on 9 April 2011. DH remains vigilant on any new safety information related to the products.

US: Updates on reports of Hepatosplenic T-Cell Lymphoma in adolescents and young adults associated with Tumor Necrosis Factor (TNF) blockers, azathioprine and/or mercaptopurine

15 April 2011 – US FDA informed the public that the Agency continued to receive reports of a rare cancer of white blood cells (known as Hepatosplenic T-Cell Lymphoma or HSTCL), primarily in adolescents and young adults being treated for Crohn's disease and ulcerative colitis with tumor necrosis factors (TNF) blockers, as well as with azathioprine, and/or mercaptopurine. In August 2009, the FDA completed a review of TNF blockers and concluded that there was an increased risk of lymphoma and other cancers associated with TNF blockers in children and adolescents. The TNF blocker labels were then revised to include this new warning. In view of the current updates, the product labels for azathioprine and mercaptopurine were being updated to include warnings about HSTCL in US.

In Hong Kong, there are 11 registered TNF blockers, 9 registered products containing azathioprine and 2 registered products containing mercaptopurine and

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all are precription medicines. In September 2009, the Registration Committee of the Pharmacy and Poisons Board, after considering the FDA's action of August 2009 related to TNF blockers, decided that the label and/or package insert of these products should be revised to include the relevant safety information. Regarding the recent safety news of FDA of April 2011 related to azathioprine and mercaptopurine, DH has already issued letters to inform healthcare professionals about this matter. In addition, after considering the relevant action of FDA at its meeting held on 11 May 2011, the Registration Committee of the Pharmacy and Poisons Board decided that the sales pack label and/or package insert of products containing azathioprine or mercaptopurine should include information about the potential risk of causing HSTCL as endorsed by the FDA. DH remains vigilant to any new findings about TNF blockers, azathioprine and mercaptopurine.

Drug Recall

Recall of Concentrated Sodium Chloride Injection

On 18 March 2011, the Department of Health (DH) instructed three licensed wholesalers, namely Hui Tai Pharmaceuticals Co. Ltd, Sino-Asia Pharmaceutical Supplies Ltd and United Italian Corporation (HK) Ltd, to recall 12 batches of Concentrated Sodium Chloride Injection, USP 23.4% because visible particulates were found in the product. The batch numbers under recall were 9299, 9305, 9402, 9432, 9553, 9595, 9646, 9681, 9737, 9797, 9831 and 0051.

The recall followed the US Food and Drug Administration (FDA)'s initiative when they detected that some of the vials of the said product exhibited translucent visible particles, consistent with glass delamination. Indeed, glass delamination can occur with high pH solutions when the surface glass from the vial separates into thin layers, resulting in glass particles with a flaky appearance. Potential adverse events after intravenous administration of the problematic product include damage to blood vessels in the lung, localised swelling and granuloma formation.

In US, the above product is distributed by a company called American Regent. The product is indicated as an additive in parenteral fluid therapy for use in patients who have special problems of sodium electrolyte intake or excretion. FDA had recalled 21 batches of the product from the US market.

In Hong Kong, record showed that 12 of the 21 affected batches have been imported via the above three named companies for supply to the Hospital Authority and three private hospitals for the treatment of particular named patients. Press statement was issued on 18 March 2011. DH closely monitored the recall. Healthcare providers in reception of the affected batches were advised to stop supplying the products further and contact the above suppliers. They were requested to report related adverse events to DH. Members of the public were advised to consult their healthcare providers when in doubt and in particular if they feel unwell after using the product.

Recall of Cebemyxine eye drops (HK-46420)

On 23 March 2011, Bausch & Lomb (Hong Kong) Ltd (B&L), a licensed drug wholesaler, initiated a recall of all batches of its Cebemyxine Eye Drops (HK-46420) due to possible quality defect. The drug is a prescription medicine containing antibiotics and is indicated for topical treatment of eye infections. It is manufactured in France.

During routine stability testing, the manufacturer found the content of one of the active ingredients, Polymyxin B, to be lower than the specified level in some batches (Batches No: E2576, E1796 and E2826). Data in France showed that the defective batches have been distributed to Morocco and Turkey. In Hong Kong, B&L's record showed that only one batch (Batch No: F1195) is available in our local market.

Although the only batch for sale in Hong Kong is not amongst those tested to be of inferior quality, B&L opted for voluntary recall of all products from consumers as a precautionary measure. The batch is known to have been supplied to local pharmacies and private doctors, and also exported to Macau. After assessment, DH endorsed B&L's decision and closely monitored the recall. Press statement was

issued on 23 March 2011 and DH has not received any adverse event report related to the use of the medicine so far. Healthcare professionals and retailers were advised to stop supplying the product to their clients. People who have used the affected product were advised to consult healthcare providers if in doubt or feeling unwell.

Recall of Lasix injection (HK-05566)

On 7 April 2011, DH instructed licensed drug wholesaler, Sanofi-Aventis Hong Kong Limited (Sanofi-Aventis), to recall 12 batches of a pharmaceutical product called "Lasix 250mg/25ml injection" (HK-05566) from market because of potential safety issue. The batch numbers of the batches under recall were 40N919, 40N934, 40N941, 40B115, 40B128, 40B149, 40U215, 40U228, 40U245, 40C311, 40C337 and 40C369. The products have been supplied to hospitals and medical practitioners.

The recall followed findings by the product's German manufacturer, Sanofi-Aventis Deutschland GMBH that during their ongoing stability tests, visible particles were found in some ampoules of certain batches produced after more than 18 months.

Among the imported batches, a total of 12 batches of the product were manufactured more than 18 months and only one batch was found to contain visible particles. DH requested Sanofi-Aventis to recall the 12 batches from the market as a precautionary measure. Press statement was issued on 7 April 2011. DH closely monitored the recall.

Healthcare providers in reception of the 12 batches were advised to stop immediately supplying the batches further. and to report related adverse events to the DH. As there is no other replacement medicines in the market, healthcare workers were reminded to be vigilant and check for visual particles before supplying and using other batches of the product to their patients. Members of the public were advised to consult their healthcare providers if in doubt or feel unwell after using the product.

Recall of Multi-12 For IV Infusion (HK-53536)

On 8 April 2011, a licensed drug wholesaler, Baxter Healthcare Limited (Hong Kong) (Baxter), initiated a recall of affected batches of Multi-12 For IV Infusion (HK-53536) as the batches were not manufactured in line with approved procedure. The recall was initiated after the product's manufacturer, Sandoz Canada, reported that it had used purified water instead of water for injection to mix an active ingredient in certain batches. Internal investigation by the manufacturer so far showed that the affected batches met other specifications, including sterility and endotoxin levels. Two affected batches (batch no. 157483 and BC7364) of the product were imported into Hong Kong and subsequently supplied to private hospitals and private practitioners. After assessment, DH endorsed Baxter's decision and closely monitored the recall. Baxter had set up a hotline for public enquiries. Press statement was issued on 8 April 2011.

Healthcare professionals were urged to stop supplying the product further, to contact the wholesaler and to report suspected adverse events. Members of the public were advised to consult their healthcare providers when in doubt and in particular if they feel unwell after having used the product. Multi-12 For IV Infusion is used in patients with need for vitamin supplement. These include those on parenteral nutrition and those after surgery, have extensive burns or fractures.

Useful Contact

Drug Complaint:

Tel: 2572 2068

Fax: 2147 0457 & 2123 1996

E-mail: pharmgeneral@dh.gov.hk

Adverse Drug Reaction (ADR) Reporting:

You are encouraged to report any suspected or confirmed ADR cases to our office by:

Fax: 2147 0457

E-mail: adr@dh.gov.hk

Post: *ADR Monitoring Unit,*

Pharmaceutical Service, Department of Health,

3/F, Public Health Laboratory Centre,

382 Nam Cheong Street, Kowloon