Drug News
藥 物 情 報

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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

Review on safety and efficacy of Avastin (bevacizumab)

Situation in the United States (US)

17 December 2010 – The US Food and Drug Administration (FDA) recommended to remove the breast cancer indication from the label for Avastin (bevacizumab). The recommendation was made after the agency had reviewed the results of four relevant clinical studies which showed that the drug neither prolonged overall survival nor provided a sufficient benefit in slowing disease progression to outweigh the significant risk to patients with breast cancer. Avastin, in combination with paclitaxel, was approved under the FDA's accelerated approval program for treatment of breast cancer in February 2008.

The drug itself is not being removed from the market and the recommendation will not have any immediate impact on its use in treating breast cancer. This action will not affect the approvals of Avastin's indication for colon, kidney, brain, and lung cancers. Oncologists who were treating patients with Avastin for metastatic breast cancer were advised to use their medical judgment when considering the therapeutic options.

The FDA is considering a submission from Genentech, Avastin's manufacturer, regarding its request for a Note of Opportunity for a Hearing received on 18 January 2011.

Situation in Europe

On 16 December 2010, the European Medicines Agency (EMA) confirmed that the benefits of Avastin in combination with paclitaxel outweigh its risks and that this combination remained a valuable treatment option for patients with metastatic breast cancer. The statement was made because the available data showed that the therapy could prolong progression-free survival of breast cancer patients without a negative effect on the overall survival.

On the other hand, the Agency's Committee for Medicinal Products for Human Use (CHMP) concluded that the benefits of Avastin in combination with docetaxel no longer outweighed its risk and recommended that this combination should no longer be used in the treatment of breast cancer.. The Committee's recommendations had been sent to the European Commission for the adoption of a decision.

Situation in Hong Kong

In Hong Kong, Avastin is registered by Roche HK Ltd. Apart from its indications for colon, kidney, brain, and lung cancers, the product is also approved to treat patients with metastatic breast cancer in combination with paclitaxel or docetaxel. This issue will be discussed in the coming meeting of Registration Committee of the Pharmacy and Poisons Board scheduled to be held on 11 May 2011.

Defects in patient information leaflets for Simvastatin 20 mg and 40 mg Tablets - of Ranbaxy (UK) Ltd in the United Kingdom (UK)

17 December 2010 – The Medicines and Healthcare products Regulatory Agency (MHRA) alerted healthcare professionals that the patient information leaflets (PIL) attached in specific batches of Simvastatin 20 mg and 40 mg Tablets of Ranbaxy (UK) Ltd had not been updated to include approved safety warnings. Some of these warnings were previously initiated by EMA and were mandatory. Due to the potential for product shortages, affected

batches were not being recalled. According to MHRA, the PIL has already been corrected and no further packs containing the incorrect PIL would enter the market.

Simvastatin is for treating hypercholesterolemia. . In Hong Kong, one of the concerned products (Simvastatin 20 mg Tablets of Ranbaxy) has been registered by a local company, Mekim Ltd. under the name of "Simvor Tab 20mg" since 2002. According to Mekim Ltd., the product has never been marketed in Hong Kong. The Department of Health (DH) has instructed the company to ensure the product insert will be updated if the product will be marketed in Hong Kong.

Detection of endotoxins in Baxter peritoneal dialysis solutions manufactured in Ireland

18 December 2010 - EMA had been informed by Baxter of the potential presence of endotoxins in their peritoneal dialysis solutions Dianeal, Extraneal and Nutrineal. These products are sterile solutions used in patients who have to undergo peritoneal dialysis because of kidney failure.

The problem was detected when Baxter found during routine testing at their Castlebar manufacturing plant in Ireland that a number of batches contained unexpected levels of endotoxins (toxic substances from bacterial cell debris). The investigation by the company revealed that two of the tanks used in the production process were found to have microscopic cracks where endotoxin-producing bacteria had settled. The tanks were then taken out of the production line and the company had reviewed its procedures to minimise the risk of the problem happening again.

After balancing the potential risk and access to treatment, the CHMP advised Baxter to set up a plan to progressively replace the potential affected batches in the market and step up its monitoring systems for prompt detection of impact on exisiting users of the presence of endotoxins in the solutions and facilitate subsequate follow-up actions. Prescribers were advised to be vigilant when considering therapy for peritoneal dialysis patients.

In Hong Kong, there are two Nutrineal products registered, one is manufactured in Ireland wheras the other is manufactured in Singapore. Both are registered by a local company, Baxter Healthcare Ltd. The company has confirmed that it is not selling Nutrineal from Ireland source in Hong Kong and it is currently only marketing Nutrineal manufactured in Singapore.

Ongoing safety review on recombinant human growth hormone (somatropin) by FDA

23 December 2010 –US FDA was reviewing all available information concerning the possible increased risk of death with the use of somatropin. The review was initiated in response to the result of a study conducted in France, the Santé Adulte GH Enfant (SAGhE), which found that persons with certain kinds of short stature (idiopathic growth hormone deficiency and idiopathic or gestational short stature) treated with recombinant human growth hormone during childhood were at a small increased risk of death over a long period of time when compared to individuals in the general population of France. At this juncture, FDA believes the benefits of recombinant growth hormone continue to outweigh its potential risks.

In Hong Kong, there are 13 registered pharmaceutical products containing somatropin. All of them are prescription medicines for treatment of children with growth failure due to pituitary growth hormone deficiency or Turner's syndrome. As reported in Issue No. 14 of Drug News, the EMA is also reviewing the safety on somatropin-containing medicines. DH has issued a letter to remind the concerned registration holders to actively report any adverse drug reaction involving the drug and report the new findings of relevant studies to DH when available. DH remains vigilant to any updates about this drug.

Recall of Gabapentin Capsules 300mg (Teva UK Ltd) in UK

23 December 2010 – In UK, Teva UK Ltd initiated a recall of all remaining stock of Gabapentin 300 mg Capsules with batch numbers 003784, 003795, 003796 and 003798 due to the discovery of a small number of capsules with low fill weights. Gabapentin is used for the treatment of partial seizures with or without secondary generalisation, and peripheral neuropathic pain.

In Hong Kong, Gabapentin Cap 300mg (TEVA) is a

prescription medicine registered by a local company, the International Medical Co. Ltd. The company confirmed that the batches recalled in UK had not been imported into Hong Kong.

Recall of one lot of Lipitor in US

December 2010 - Further to the previous recalls of specific batches of Lipitor 40 mg Tablets (atorvastatin calcium) in August, October and November 2010 in US, Pfizer initiated another recall of a specific lot of the product distributed in the State. The recalls stemed from a customer report of an uncharacteristic odour related to the bottles supplied by a third-party manufacturer for packing of Lipitor. A medical assessment had determined that the odour was not likely to cause adverse health consequences in patients taking Lipitor.

In Hong Kong, Lipitor is registered by Pfizer Corporation Hong Kong Limited for the treatment of hypercholesterolemia. Pfizer confirmed that all Lipitor marketed in Hong Kong was packed in blister only.

No evidence of an increased risk of febrile convulsions in children following seasonal flu vaccination in UK

24 December 2010 – In response to a report of an excess risk of febrile convulsions associated with a brand of flu vaccine (Fluvax, manufactured by CSL) in Australia, which was published in Issue No. 7 and No. 9 of Drug News, the Medicines and Healthcare products Regulatory Agency (MHRA) monitored reports of febrile convulsions in this year's UK flu vaccination campaign. It was found that cases of febrile convulsion reported this year in the UK with other (non-CSL/Pfizer) vaccines were within the usual range, and that there was no indication of an excess risk of febrile convulsions in children following seasonal flu vaccination.

As reported in the previous issues of Drug News, the concerned vaccine, Fluvax, is registered by a local company, Luen Cheong Hong Ltd in Hong Kong. The company had confirmed that the Fluvax is solely for the southern hemisphere and had not been imported into Hong Kong. The company was instructed to ensure that the safety information related to febrile convulsions would be included in the package insert before the vaccine would be marketed in Hong Kong.

Ongoing safety review of Lantus (insulin glargine) in US

13 January 2011 - US FDA annouced the progress of its safety review on a possible increased risk of cancer with Lantus (insulin glargine). Lantus is a long acting recombinant human insulin analogue used for the treatment of diabetes mellitus. In July 2009, the FDA made a public announcement that the agency was reviewing four published observational studies, three of which suggested an increased risk of cancer associated with the use of Lantus. The review of 2009 was completed and the FDA remarked that the evidence presented in the studies was inconclusive because of the methodological limitations and insufficient data for sound analysis. The present review is still in progress and the Agency will update the public when it has additional information.

The safety of Lantus had also been reviewed by the EMA since 2009. In May 2010, the Agency's CHMP considered the the benefit-risk balance of Lantus remained positive but its safety profile should be closely monitored by requesting yearly Periodic Safety Update Reports from the Marketing Authorization Holder.

In Hong Kong, Lantus is registered by Sanofi-Aventis Hong Kong Ltd. DH remains vigilant to any updates about this issue.

Imposing dosage strength limit and liver toxicity warning label on prescription combination products containing acetaminophen in US

14 January 2011 – To reduce the risk of liver injury from unintentional acetaminophen overdose, US FDA was requesting relevant manufacturers to limit the amount of acetaminophen in prescription combination products containing acetaminophen to no more than 325 mg in each tablet or capsule and to add a boxed warnings to the labels of these products to address the potential risk of severe liver damage.

Acetaminophen, also called APAP, is a drug that relieves pain and fever and can be found in both prescription and over-the-counter (OTC) products. It commonly combines with other ingredients, usually opioids such as codeine (Tylenol with Codeine), oxycodone (Percocet), and hydrocodone (Vicodin) in many prescription products. OTC acetaminophen

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products are not affected by FDA's action. Drug companies will have three years from the date of publication of the Federal Register Notice (14 January 2011) to comply with the requirement in dosage limitation.

In view of concerns over the reports of serious liver damage secondary to acetaminophen overdose, Health Canada had also finalized a new labeling standard for non-prescription products containing acetaminophen in September 2009. The labeling standard contained warning of potential serious and possibly fatal liver damage in the event of an overdose. All products concerned in Canada were expected to have complied with the new labelling standard by Fall 2010.

In Hong Kong, there are 10 registered pharmaceutical products containing acetaminophen in combination with opioids. Most of them are prescription medicines. In light of the new labelling requirement of FDA, DH issued letters to healthcare professionals to inform them about FDA's decision on 14 January 2011 and reminded them to prescribe acetaminophen safely and advise patients accordingly. In this connection, Registration Committee of the Pharmacy and Poisons Board decided at its meeting held on 15 February 2011 that the sales packs labels of the products should include appropriate statements to-

i) highlight the potential for liver toxicity and severe liver damage;

ii) advise against using more than the recommended dose of acetaminophen; and

iii) advise against using more than one product containing acetaminophen.

On 16 February 2011, DH issued a letter to inform the concerned registration holders to review the sales pack labels of their products containing acetaminophen and take appropriate actions to ensure the above requirements are complied with within 2 months from the date of the letter.

Risk of severe liver Injury associated with dronedarone (Multaq)

15 January 2011 – US FDA alerted healthcare professionals and patients about rare cases of severe liver injury, including two cases of acute liver failure leading to liver transplant, in patients treated with dronedarone (Multaq). Dronedarone is an anti-arrhythmic drug indicated to reduce the risk of cardiovascular hospitalization in patients due to atrial fibrillation or atrial flutter.

In US, information about the potential risk of liver injury from dronedarone was added to the WARNINGS AND PRECAUTIONS and ADVERSE REACTIONS sections of the dronedarone labels. Healthcare professionals were advised to check hepatic serum enzymes periodically, especially during the first 6 months of treatment, and to alert patients taking dronedarone about the signs and symptoms of hepatic injury.

In Hong Kong, Multaq tablet is registered by Sanofi-Aventis HK Ltd., and is a prescription medicine. The company had informed the DH about the mentioned two cases of acute liver failure overseas, and would revise the package insert by including the appropriate warning messages. DH has issued letters to healthcare professionals to alert them about this matter on 15 January 2011.

Drug Recall

Recall of Vita Prima B1+B6+B12 Tablets

On 28 December 2010, Julius Chen & Co. (HK) Ltd. (Julius Chen), a licensed drug wholesaler, initiated a recall of Vita Prima B1+B6+B12 Tablet (HK-53232, batch no. 3027700) from the market because bottle label of the product showed an incorrect strength.

The recall was initiated after Julius Chen found that the content of Vitamin B-12 (Cyanocobalamin) mentioned in the product label on the bottle was incorrectly printed as ***200mg*** while the correct content should be ***200mcg***. However, the external packing of the product was correctly labelled. Although the issue would not cause immediate safety, quality and efficacy concern, Julius Chen opted for voluntary recall as a precautionary measure. After assessment, DH endorsed Julius Chen's decision and closely monitored the recall.

Vita Prima B1+B6+B12 Tablet, a non-prescription medicine containing Vitamin B-1(Thiamine HCl), Vitamin B-6 (Pyridoxine HCl) and Vitamin B-12 (Cyanocobalamin), is used for the treatment of Vitamin B1, B2 and B12 deficiency.

Drug Incidents

Man arrested for selling product with banned drug ingredient

On 29 December 2010, DH appealed to members of the public not to buy or consume products of unknown or doubleful sources advertised on the internet as they might contain undeclared drug ingredients that are dangerous to health.

The appeal followed the arrest of a man aged 20 in a joint operation by the Police and DH for suspected sale of a product which was known to cotain an undeclared banned drug. The product's name was "Chalkiness Cap".

The Department previously obtained the product concerned from an internet auction website during the Department's surveillance operation. Laboratory test revealed that the product contained the banned drug, phenolphthalein, which was once used for treating constipation but has been banned since 2001 for its cancer-causing effect.

Public urged not to use consumer product containing controlled ingredient

On 11 January 2011, DH urged members of the public not to use a slimming product called "CM Factor" as it was found to contain a controlled ingredient.

The appeal followed the Department's investigation into a public enquiry regarding the above product. A product sample was subsequently purchased from a retail shop at Causeway Bay in December 2010. Laboratory analysis revealed the presence of a sibutramine analogue in the product. The Department mounted an operation on 11 January 2011, resulting in the seizure of 815 boxes of C M Factor from the wholesaler and the retail shop concerned.
In fact, the product has previously been found to contain the western drug sibutramine and a public announcement was issued on 9 April 2009.

Sibutramine was once used for treatment of obesity. Products containing sibutramine has been banned since November 2010 for its risk of serious cardiovascular side-effects. Sibutramine analogues, being chemically similar to sibutramine, are expected to have the same side effect as sibutramine.

Weight control should be achieved through healthy diet and appropriate exercise. People should consult healthcare professionals before using any medication for weight control.

The products mentioned in the above drug incidents were not registered pharmaceutical products under the Pharmacy and Poisons Ordinance in Hong Kong. A product containing any western drug ingredient must be registered under the Ordinance before it can be sold in Hong Kong. Under the Pharmacy and Poisons Ordinance, possession or sale of unregistered pharmaceutical product is an offence liable to the maximum penalties of a $100,000 fine and two year's imprisonment.

Members of the public were exhorted not to sell products of unknown or doubtful composition. Members of the public should stop using the aforementioned products that contained undeclared western drug ingredients and they should see doctors if they feel unwell after using the products. They should destroy, dispose or submit them to the Department's Pharmaceutical Service during office hours.

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