



# Drug

藥

物

# News

情

報

**Issue No. 10 : August 2010**

*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

### Ongoing safety review of the angiotensin receptor blockers and cancer by the United States Food and Drug Administration

15 July 2010 – The United States Food and Drug Administration (FDA) has initiated a review of the class of medications known as angiotensin receptor blockers (ARBs) after a recently published study suggested they might be associated with a small increased risk of cancer. ARBs are used in high blood pressure and other conditions, they include candesartan, irbesartan, olmesartan, losartan, valsartan, telmisartan and eprosartan. The meta-analysis included data from over 60,000 patients in several long-term, randomized, controlled clinical trials evaluating ARBs for which adverse events related to cancer were captured during the study. The mean duration of follow-up ranged from 1.7 to 4.8 years. The study reported the frequency of new cancer occurrence to be 7.2% for patients receiving ARBs compared to 6.0% for those not receiving ARBs (risk ratio = 1.08, 95% Confidence Interval: 1.01-1.15). No statistically significant difference in cancer deaths was noted. However, the FDA commented that the meta-analysis had several limitations that make it difficult to determine the validity of the findings without further examination of the underlying data. At this time, FDA believes that the benefits of these medicines continue to outweigh their potential risks. FDA recommended that healthcare professionals can continue to use ARBs as recommended in their product labels.

Products containing angiotensin receptor blockers are available in Hong Kong. The Department of Health remains vigilant to any new findings about this class of drugs.

### European Medicines Agency updated on

### ongoing benefit-risk review of rosiglitazone (Avandia, Avandamet and Avaglim)

22 July 2010 – The Issue no. 7 of Drug News has reported the Medicines and Healthcare products Regulatory Agency in United Kingdom concerns over the cardiovascular safety of the products containing rosiglitazone. Rosiglitazone is a thiazolidinedione for treatment of type II diabetes. Further to the report, the European Medicines Agency (EMA) has initiated a review of rosiglitazone to determine the impact of new data from recent publications on the benefit- risk profile of the products containing the medicine, namely Avandia, Avandamet and Avaglim. The EMA noted that additional new data sets had become available very recently. It would assess these data in depth together with all other available data on the benefits and risks of rosiglitazone. Prescribers in the European Union were reminded to strictly follow the recommendations in the product information with respect to patients indicated for treatment, defined contraindications and warnings. Doctors should pay particular attention to the following:

- rosiglitazone must not be used in patients with current or previous heart failure and in patients with acute coronary syndrome;
- rosiglitazone and insulin should only be used together in exceptional cases and under close supervision; and
- the use of rosiglitazone is not recommended in patients with ischaemic heart disease or peripheral arterial disease.

Among the above three products, only Avandia and

## Safety Update

Avandamet are registered in Hong Kong. The above safety information has been included in the package inserts of the two products. The Department of Health remains vigilant to any new findings about rosiglitazone.

### **European Medicines Agency confirmed positive benefit-risk balance of topical formulations of ketoprofen, a medicine for pain relief**

22 July 2010 - Following a review of topical formulations of ketoprofen, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) had concluded that the benefit-risk balance of these medicines continues to be positive. The review of these medicines had been initiated further to concerns over the risk of skin photosensitivity reactions, including photoallergy, and a new risk of co-sensitization with octocrylene (a chemical sun filter included in several cosmetic and care products). The Committee recommended that topical ketoprofen should only be used when prescribed by a physician. The CHMP also recommended strengthening the contra-indications and warnings on sun exposure and a warning on the risk of co-sensitisation when used together with octocrylene-containing products.

In Hong Kong, topical products containing ketoprofen are registered as plasters, patches and gels. They are prescription medicines and used for pain relief in joints and muscles. Department of Health has issued a press statement and a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information. In addition, the issue will be considered by the Registration Committee of the Pharmacy and Poisons Board in the upcoming meeting.

### **European Medicines Agency confirmed positive benefit-risk balance of Rotarix, a rotavirus vaccine**

22 July 2010 – On 22 March 2010, the European Medicines Agency was aware of the unexpected presence of DNA of a non-disease causing viral strain in batches of the oral vaccine Rotarix by the GlaxoSmithKline Biologicals. An initial review by the Agency's Committee for Medicinal Products for Human Use (CHMP) considered that the findings

did not present a public health threat. After further review, the CHMP later had concluded that the vaccine would continue to have a positive benefit-risk balance and that the presence of a very small amount of viral particles would not present a risk to public health. Data from tests carried out by the manufacturer, GlaxoSmithKline Biologicals S.A., showed that the vaccine contained only very small amounts of live PCV-1. The viral particles might have always been present in the vaccine, and have been found in the raw material used to make the vaccine. Their presence was detected only now because of the emergence of new technology.

In Hong Kong, 2 rotavirus vaccines, namely Rotarix (registered by GlaxoSmithKline Ltd) and RotaTeq (registered by Merck Sharp & Dohme (Asia) Ltd.) were once recalled in March and May 2010 respectively as a precautionary measure following the report of discovery of PCV-1 in Rotarix and PCV-1 and PCV-2 in RotaTeq by the respective manufacturers. However, after review and examination of available information, the Department of Health (DH) has concluded that the benefits of these vaccines outweigh the risks. Both vaccines have been resumed for use later in May 2010. The package insert of Rotarix has been revised to include information on the presence of the viral particles whereas that of RotaTeq is being revised. DH has issued press statements and "Dear Healthcare Professionals" letters to doctors to update the public and healthcare professionals above the developments the two rotavirus vaccines. DH remains vigilant to any new findings about rotavirus vaccines.

### **Risk of rhabdomyolysis associated with the use of lamivudine and telbivudine issued by the State Food and Drug Administration, China**

22 July 2010 - A news bulletin published by the State Food and Drug Administration, China reminded doctors about the risk of rhabdomyolysis associated with the use of lamivudine and telbivudine. Rhabdomyolysis is a serious muscle injury, it occurs when muscle fibers break down and release a protein (myoglobin) which may damage the kidneys. Lamivudine and telbivudine are both used for treatment of chronic hepatitis B infection. Lamivudine is also used in combination with other antiviral agent for the treatment of HIV infection.

## Safety Update

Products containing lamivudine and telbivudine are available in Hong Kong. Department of Health has issued a press statement and a “Dear Healthcare Professionals” letter to inform healthcare professionals about this safety information. This issue will be considered by the Registration Committee of the Pharmacy and Poisons Board in the upcoming meeting.

### **European Medicines Agency concluded review of modified-release oral opioids of the WHO level III scale for the management of pain**

23 July 2010 - The European Medicines Agency had finalised a review of modified-release oral opioids of the WHO level III scale for the management of pain. They included morphine and the related medicines oxycodone and hydromorphone. They are called ‘WHO level III scale’ medicines as they are on the highest step of the World Health Organization’s three-step pain relief ladder. This ladder gives recommendations on the order in which painkillers of increasing strength should be used to control a patient’s pain.

These medicines were reviewed because of concerns that their controlled-release systems might be unstable in alcohol and that the active substance might be released too quickly when patients took them together with alcohol. This effect called ‘dose dumping’ could put patients at risk of exposure to large doses of the opioid, which might lead to serious side effects such as respiratory depression (an inhibition of breathing). Based on the evaluation of the available data, the Agency’s Committee for Medicinal Products for Human Use (CHMP) found that around half of the controlled-release systems tested interacted with alcohol, but that this effect was mild and would only have a minor effect on the release of the active substance. However, for opioids using a polymethacrylate-triethylcitrate controlled-release system, the CHMP found that there was a significant interaction with alcohol and that patients were at risk of dose dumping if they drank alcohol while taking them.

The CHMP recommended to suspend the marketing authorisations of modified-release oral opioids that contain a polymethacrylate-triethylcitrate controlled-release system until the manufacturers have reformulated them so that they are more stable in alcohol. For other modified release oral opioids of

WHO level III, the CHMP concluded that the benefits continue to outweigh their risks, but that the existing warnings on the interaction of these medicines with alcohol e.g. the increased sedative effects of opioids should be made consistent across the class.

In Hong Kong, modified-release oral opioids including morphine and oxycodone are registered in HK. However there is no modified-release oral opioids that contains a polymethacrylate-triethylcitrate controlled-release system registered in HK. Regarding the existing warnings on the interaction of opioids with alcohol, the issue will be considered by the Registration Committee of the Pharmacy and Poisons Board in the upcoming meeting.

### **Eosinophilic pneumonia associated with the use of Cubicin (daptomycin) reported by the United States Food and Drug Administration**

29 July 2010 - The United States Food and Drug Administration (FDA) notified healthcare professionals and patients about the potential for developing eosinophilic pneumonia during treatment with Cubicin (daptomycin), an intravenous antibacterial drug indicated for use in treatment of serious skin infections and bloodstream infections. FDA’s review identified 7 cases of eosinophilic pneumonia between 2004 and 2010 that were most likely associated with Cubicin. Based on these reviews, FDA determined that eosinophilic pneumonia could be associated with Cubicin use and requested that the manufacturer of Cubicin to include this information in the package insert.

In Hong Kong, Cubicin is registered by AstraZeneca Hong Kong Ltd. In the current package insert, post-marketing reports of cases of pulmonary eosinophilia has been mentioned. The company confirmed to update the insert as recommended by FDA. Department of Health has issued a “Dear Healthcare Professional” letter to doctors reminding them to closely monitor patients who are using Cubicin for signs and symptoms of eosinophilic pneumonia. In patients exhibiting signs and symptoms of eosinophilic pneumonia, discontinue Cubicin and consider treating as clinically indicated.

## Safety Update

### **Association of Relistor (methylnaltrexone bromide) subcutaneous injection with gastrointestinal (GI) perforation reported by Health Canada**

3 August 2010 - Wyeth Canada (a Pfizer Company) informed healthcare professionals of important new safety information added to the product monograph for Relistor (methylnaltrexone bromide) subcutaneous injection. Relistor is indicated for the treatment of opioid-induced constipation in patients with advanced illness who are receiving palliative care. Patients with advanced illness being treated with Relistor may be at increased risk of GI perforation if they have conditions associated with localized or diffused reduction of structural integrity in the GI wall, these include conditions such as cancer, GI malignancy, GI ulcer, Ogilvie's syndrome, and concomitant medications (e.g. bevacizumab, nonsteroidal anti-inflammatory drugs and steroids). The risks and benefits of Relistor treatment should be weighed for each patient. Relistor should be used with caution in patients with known or suspected GI lesions.

In Hong Kong, Relistor is registered by Wyeth (HK) Ltd. The company confirmed that Relistor has not been imported into Hong Kong since its registration firstly approved in July 2009; and the company has been instructed to update its package insert with the above safety information before Relistor is marketed in Hong Kong.

### **Risk of severe skin reactions associated with the use of isotretinoin, a medicine for acne treatment, issued by the State Food and Drug Administration, China**

11 August 2010 - A news bulletin published by the State Food and Drug Administration (SFDA), China, reminded doctors about the risk of erythema multiforme, Stevens-Johnson Syndrome and toxic epidermal necrolysis associated with the use of isotretinoin. The Roche global safety database had found 66 cases of severe skin reactions including erythema multiforme, Stevens-Johnson Syndrome and toxic epidermal necrolysis in association with their product, Roaccutane. European Medicines Agency had also reviewed this issue, and concluded that a relationship with erythema multiforme was confirmed, but not confirmed for Stevens-Johnson Syndrome and toxic epidermal necrolysis. The

SFDA also cautioned doctors of other risks associated with isotretinoin including teratogenicity, severe psychiatric symptoms, changes in lipid levels and intracranial hypertension.

Products containing isotretinoin are registered in Hong Kong. Department of Health has issued a "Dear Healthcare Professionals" letter to remind healthcare professionals about this safety information. This issue will be considered by the Registration Committee of the Pharmacy and Poisons Board in the upcoming meeting.

### **Aseptic meningitis risk with use of seizure drug Lamictal issued by the United States Food and Drug Administration**

12 August 2010 - The United States Food and Drug Administration (FDA) warned that the drug Lamictal (lamotrigine), approved to treat seizures and bipolar disorder, can cause aseptic meningitis, an inflammation of the protective membranes (meninges) that cover the brain and spinal cord not caused by bacterial infection. Since the drug's approval in December 1994 through November 2009, there were 40 cases of aseptic meningitis identified in patients taking Lamictal. The symptoms were reported to occur within one to 42 days after starting Lamictal. Thirty-five of the 40 patients required hospitalization. In most cases, symptoms ended after Lamictal was discontinued. In 15 cases, symptoms, often more severe, returned when patients restarted the drug. In suspected cases of meningitis, the underlying cause should be rapidly diagnosed so that treatment can be promptly initiated. Discontinuation of Lamictal should be considered if no other clear cause of meningitis is identified. The agency was working with the drug's manufacturer, GlaxoSmithKline, to update the prescribing information and patient medication guide to include this risk.

Lamictal, by GlaxoSmithKline Ltd, and other generic lamotrigine products are available in Hong Kong. Department of Health has issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information. This issue will be considered by the Registration Committee of the Pharmacy and Poisons Board in the upcoming meeting.



## Drug Recall

### Recall of pharmaceutical products – B-Com Forte Syrup (HK-05440) and B-Com Syrup (HK-17496)

On 26 July 2010, drug manufacturer Neochem Pharmaceutical Laboratories Ltd (Neochem) recalled all batches of B-Com Forte Syrup and B-Com Syrup because analytical results showed that one of the labelled ingredients, Vitamin B1, was not detected in the sample of B-Com Forte Syrup. Both B-Com Forte syrup and B-Com syrup shared the same formula. Although the laboratory finding

pointed to quality defects, nevertheless, Neochem recall the products as a precaution.

The products were only produced in bulk pack of 3.6L and they had been supplied to medical practitioners and some pharmacies. Neochem had set up a hotline for public enquiries.

Department of Health has issued a press statement to urge healthcare professionals and retailers to stop supplying the products to their clients. Patients should consult healthcare professionals if in doubt.

## Drug Incident

### Public was urged not to use of “[Zhang Guang] Gold 101 Super Effective Hair Growth Agent and [101 Zhangguang] Zhangguang 101D Fabao” with undeclared western drug ingredient

On 2 August 2010, the Department of Health (DH) issued a press statement to urged the public not to buy or use two haircare products registered as proprietary Chinese medicines called “[Zhang Guang] Gold 101 Super Effective Hair Growth Agent 「章光 1 0 1」金裝 1 0 1 高級生髮靈” (Registration number: HKP-08408)” and “[101 Zhangguang] Zhangguang 101D Fabao「章光」章光 1 0 1 D 髮寶” (Registration number: HKP-07223) as they were found to have contained a western drug ingredient, minoxidil. DH inspected the two wholesalers and instructed them to recall the products from the market. It was followed the detection of minoxidil in the products during the DH’s surveillance programme.

Both products are manufactured in the Mainland by "Beijing Zhangguang 101 Science & Technology Development Co. Ltd". They were imported by two local licensed wholesalers. The wholesalers have set up hotlines to answer enquiries about the recall.

Minoxidil is a western medicine used for the treatment of hair loss. Its side effects include skin irritation, rash and itchiness. Products containing minoxidil can be sold in registered pharmacies under the supervision of a pharmacist.

The aforementioned products 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 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.

### *Useful Contact*

#### Drug Complaint:

**Tel: 2572 2068**

**Fax: 2147 0457 & 2123 1996**

**E-mail: [pharmgeneral@dh.gov.hk](mailto: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: 2572 4570**

**E-mail: [adr@dh.gov.hk](mailto:adr@dh.gov.hk)**

**Post: ADR Monitoring Unit,**

**Pharmaceutical Service, Department of Health,  
3/F, Public Health Laboratory Centre,  
382 Nam Cheong Street, Kowloon**