Drug News
藥 物 情 報

Issue No. 11 : September 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

United States Food and Drug Administration proposed withdrawal of midodrine hydrochloride

16 August 2010 - The United States Food and Drug Administration (FDA) proposed to withdraw the approval of midodrine hydrochloride, a drug used in the treatment of a low blood pressure condition, orthostatic hypotension. The drug was approved in the United Stated in 1996 under the FDA's accelerated approval regulations for drugs that treat serious or life-threatening diseases. That approval required the manufacturers to verify clinical benefit to patients through post-approval studies, but the required post-approval studies have not been done by the manufacturers.

Currently, there are two products containing midodrine hydrochloride registered in Hong Kong. The Department of Health remains vigilant to any new development about this drug.

Reports on the lack of efficacy of Marcain (bupivacaine) during spinal anaesthesia in Singapore

16 August 2010 - The Health Sciences Authority (HSA) in Singapore had received reports on the lack of efficacy associated with the use of Marcain (bupivacaine) from AstraZeneca when used during spinal anaesthesia, but analytical results conducted on the affected batch indicated that the bupivacaine content was within specifications. Based on the HSA's review, a number of factors may contribute to the occurrence of the failed spinal anaesthesia, and HSA would continue to monitor this situation.

In Hong Kong, Marcain is registered by AstraZeneca Hong Kong Ltd as a local anaesthetic which can also be used in spinal anaesthesia. There has been no report received by the Department of Health regarding the lack of efficacy of Marcain. The Department of Health remains vigilant to any new finding about this drug.

Ongoing safety review of Stalevo and possible increased cardiovascular risk by the United States Food and Drug Administration

20 August 2010 - The United States Food and Drug Administration (FDA) notified healthcare professionals that FDA was conducting an ongoing safety review for Stalevo (combination of carbidopa, levodopa and entacapone) as study suggested that the drug may be associated with at an increased risk for cardiovascular events (heart attack, stroke, and cardiovascular death) compared to those taking carbidopa and levodopa. Stalevo is used in the treatment of Parkinson's disease. A meta-analysis based on 15 clinical trials reported an imbalance in the number of myocardial infarctions in patients treated with Stalevo compared to those receiving only carbidopa and levodopa. However, several factors in the study design made evaluation of the finding difficult. FDA is exploring additional ways to assess whether Stalevo increases the risk of cardiovascular events, and will update the public when this review is complete. Healthcare professionals should regularly evaluate the cardiovascular status of patients who are taking Stalevo, especially if they have a history of cardiovascular disease.

In Hong Kong, Stalevo is registered by Novartis Pharmaceuticals (HK) Limited and cautions regarding the use of this drug in patients with ischemic heart disease, severe cardiovascular disease or history of myocardial infarction have already been included in the package insert of this product. Monitoring of cardiac function is also

recommended during the period of initial dosage adjustment and during extended therapy. The Department of Health remains vigilant to any new finding about this drug.

Important safety information on Avastin (bevacizumab) reported by Health Canada

23 August 2010 –Hoffmann-La Roche Limited (Roche) of Canada informed healthcare professionals that hypersensitivity reactions and infusion reactions had been identified as risks in patients treated with Avastin which is used in the treatment of metastatic colorectal caner, metastatic breast cancer, advanced, metastatic or recurrent non-small cell lung cancer, advanced and/or metastatic renal cell cancer and glioblastoma. In clinical trials, anaphylactic and anaphylactoid-type reactions were reported more frequently in patients receiving Avastin in combination with chemotherapy than with chemotherapy alone. The incidences of these reactions in clinical trials of Avastin were common (up to 5% in Avastin-treated patients).

In Hong Kong, Avastin is registered by Roche Hong Kong Ltd. Similar report about the association of hypersensitivity reactions and infusion reactions has been announced by Health Sciences Authority (HSA) of Singapore in March 2010 and Department of Health had issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about the safety information at that time. Furthermore, this safety information has subsequently been added in the package insert of this product. The information was reported in the Issue No. 6 of Drug News. The Department of Health remains vigilant to any new finding about this drug.

Association of Actemra (tocilizumab) with anaphylaxis

26 August 2010 - Roche Hong Kong Ltd informed the Department of Health about an overseas report of a post-marketing fatal anaphylaxis case associated with the use of Actemra (tocilizumab), a registered intravenous drug mainly used in combination with methotrexate for the treatment of moderate and severe active rheumatoid arthritis. An elderly woman in the United States died of the anaphylactic event after the fifth infusion of Actemra. This was the first reported case of fatal anaphylaxis in a patient treated with Actemra. Clinically significant hypersensitivity reactions associated with Actemra and required treatment discontinuation had been reported in 0.3% of all patients receiving tocilizumab in its clinical trials.

Department of Health has issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information and to remind them to exercise extra caution when prescribing and supplying this drug to their patients. If an anaphylactic or other serious hypersensitivity reaction occurs following administration of Actemra, the drug should be stopped immediately. Appropriate medical management should be initiated and Actemra should be permanently discontinued in the affected patients.

GlucaGen Hypokit being recalled in Canada

25 August 2010 - Health Canada informed Canadians that Novo Nordisk Canada Inc. agreed to voluntarily recall two lots (YW60335 and YW60351) of GlucaGen Hypokit. GlucaGen Hypokit contains glucagon which is used in the treatment of severe hypoglycaemic reactions. It is supplied with a vial of lyophilized glucagen and a pre-filled water for injection syringe. The recall was initiated due to the identification of cracks in a pre-filled few water for injection syringes. According to Health Canada, no adverse reaction was received from the use of the concerned lots.

In Hong Kong, GlucaGen Hypokit is registered by Novo Nordisk Hong Kong Ltd. Other than the above two lots recalled in Canada, the company notified the Department of Health that some other affected lots had also been distributed to other countries. The company also confirmed that only one of the affected lots (YW60358) has been imported into Hong Kong; but it has not been distributed into the local market.

Updated Tygacil drug label to include information regarding increased mortality risk in the United States

1 September 2010 - The United States Food and Drug Administration (FDA) reminded healthcare professionals of an increased mortality risk associated with the use of the intravenous antibacterial, Tygacil (tigecycline), compared to that of other drugs used to treat a variety of serious

infections. The increased risk was determined by using pooled analysis of clinical trials. The cause of excess death in these trials was often uncertain but was seen most clearly in patients treated for hospital -acquired pneumonia, especially ventilator-associated pneumonia. It was also seen in patients with complicated skin and skin structure infections, complicated intra-abdominal infections and diabetic foot infections. The FDA had updated sections of the Tygacil drug label to include information regarding increased mortality risk of Tygacil and it had also recommended that alternatives to Tygacil should be considered in patients with severe infections.

In Hong Kong, Tygacil is registered by Wyeth (HK) Ltd. The approved indications of Tygacil in Hong Kong include complicated skin and skin structure infections, complicated intra-abdominal infections, and community acquired pneumonia. Tygacil is not approved for use in hospital-acquired pneumonia. The company is in the process of updating the package insert of Tygacil to include a warning regarding the increased risk of mortality. The Department of Health has issued a "Dear Healthcare Professionals" letter to inform healthcare professionals about this safety information.

New warnings required on use of gadolinium-based contrast agents by the United States Food and Drug Administration

9 September 2010 - The United States Food and Drug Administration (FDA) required that gadolinium-based contrast agents (GBCAs) carried new warnings on their labels about the risk of a rare and potentially fatal condition known as nephrogenic systemic fibrosis (NSF) if the drug is administered to certain patients with kidney disease. GBCAs are intravenous drugs approved by the FDA for use with magnetic resonance imaging or magnetic resonance angiography to help detecting abnormalities of body organs, blood vessels, and other tissues. NSF has not been reported in patients with normal kidney function. Patients at greatest risk for developing NSF after receiving GBCAs are those with impaired elimination of the drug, including patients with acute kidney injury (AKI) or chronic, severe kidney disease (with a glomerular filtration rate or GFR < 30 mL/min/1.73m^2). Higher than recommended doses or repeat doses of GBCAs also appear to increase the risk for NSF.

Three of the GBCAs – Magnevist (gadopentetic acid), Omniscan (gadodiamide), and Optimark (gadoversetamide) – were described as inappropriate for use among patients with acute kidney injury or chronic severe kidney disease. All GBCA labels would emphasize the need to screen patients to detect these types of kidney dysfunction before administration. The FDA's review of the safety of the most widely used GBCAs determined that Magnevist, Omniscan, and Optimark were associated with a greater risk than other GBCAs for NSF in certain patients with kidney disease. Data suggested that NSF may follow the administration of any GBCA and the FDA continues to assess the safety of each GBCA to better estimate its NSF risks.

In Hong Kong, GBCAs are available in Hong Kong and they include Magnevist and Omniscan, two of the three agents determined by FDA to be associated with a greater risk for NSF than other GBCAs. The others GBCAs available in Hong Kong are Gadovist (gadobutrol), Primovist (gadoxetic acid), Dotarem (gadoteric acid) and MultiHance (gadobenate dimeglumine). The current package inserts of the available GBCAs have included precautions in patients with severe kidney problems in response to similar news reported worldwide in 2007. Department of Health is working with the companies to further update their package inserts. In addition, following the above latest update of the US FDA in September 2010, the Department of Health has issued a "Dear Healthcare Professionals" letter to inform healthcare professionals accordingly.

United States Food and Drug Administration statement on ASBMR report: Possible increased risk of certain types of thigh bone fractures with long-term bisphosphonates use

14 September 2010 - A report from the American Society of Bone and Mineral Research's (ASBMR's) in the United States was released on the potential association between long term use of bisphosphonates and atypical fractures of the thigh bone. Since the initial report of unusual fractures with bisphosphonates was published, the FDA had been diligently monitoring this issue. FDA had started to review all the scientific data available regarding their safety and effectiveness when used for more than three to five years for the treatment

Safety Update

and prevention of osteoporosis. FDA would keep the public informed of additional findings and actions on this issue.

Bisphosphonate products including alendronate, clodronate, ibandronic acid, pamidronate, risedronate sodium and zoledronic acid are available in Hong Kong. The Department of Health remains vigilant to any new finding about this class of drug and will keep monitoring of any adverse drug events associated with them. The issue will be considered in the meeting of the Registration Committee of Pharmacy and Poisons Board scheduled to be held in December 2010.

Drug Recall

Voluntary recall of Panadol for Children Tablet (HK-31209) due to a mismatch of dosage instructions

On 31 August 2010, GlaxoSmithKline Ltd. (GSK), a licensed drug wholesaler, initiated a recall of a batch of Panadol for Children Tablet Chewable 120mg (Batch no.: XPH026) from the market due to a mismatch of dosage instructions between the product's package insert and carton.

The recall was initiated after GSK found that the package insert of the concerned batch carried currently registered dosage instructions based on a child's age while the carton provided new dosage instructions based on a child's weight. Although the new dosage instructions have received approval-in-principle of Department of Health (DH), it may only be used on the condition that the package insert has been changed to the new dosage instruction format and its commencement date has been agreed by DH.

The old and new dosage instructions are considered appropriate but the new instructions are more refined, taking into account the child's actual body weight instead of just his/ her age. Although there was neither safety nor efficacy concern, GSK opted for voluntary recall so as to avoid confusion. On assessment, the DH endorsed GSK's decision and would closely monitor the exercise and the development. GSK had set up a hotline for public enquiries.

DH has issued a press statement to urge healthcare professionals and retailers to stop supplying the concerned batch to their clients. People who have used the product should consult healthcare professionals if in doubt.

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: 2572 4570

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