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(IN REPLY PLEASE QUOTE THIS FILE REF.)

DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION
3/F., Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon, Hong Kong

BY FAX

2 May 2013

Dr. Donald LI
President
Hong Kong Academy of Medicine
(Fax Number: 2505 5577)

Dear Dr. LI,

Safety alerts on Samsca (Tolvaptan) announced by US FDA and on Carbamazepine announced by Singapore HSA

Your attention is drawn to the following drug safety alerts announced by US Food and Drug Administration (FDA) and Singapore Health Sciences Authority (HSA):

1. Samsca (Tolvaptan) – Limitations on the duration and usage due to possible liver injury

FDA had determined that Samsca (tolvaptan) should not be used for longer than 30 days and should not be used in patients with underlying liver disease because it can cause liver injury, potentially requiring liver transplant or death. An increased risk of liver injury was observed in recent large clinical trials evaluating Samsca for a new use in patients with autosomal dominant polycystic kidney disease (ADPKD), which had been mentioned in our previous letter issued on 28 January 2013 (http://www.drugoffice.gov.hk/eps/upload/eps_news/19190/EN/2/28-01-2013.pdf).

FDA had worked with the manufacturer to revise the Samsca drug label to include the following information:

1. Limitation of the duration of Samsca treatment to 30 days.
2. Removal of the indication for use in patients with cirrhosis, a condition that involves scarring of the liver due to injury or long-term disease. Use of Samsca in patients with underlying liver disease, including cirrhosis, should be avoided because the ability to recover from liver injury may be impaired.
3. Description of liver injuries seen in clinical trials of patients with autosomal dominant polycystic kidney disease (ADPKD).
4. Recommendation to discontinue Samsca in patients with symptoms of liver injury.

Please refer to FDA's website for details:
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm350185.htm

In Hong Kong, there are two registered pharmaceutical products containing tolvaptan, namely Samsca Tab 15mg (HK-59910) and Samsca Tab 30mg (HK-59911). They are prescription-only medicines and are indicated for the treatment of clinically significant hypervolemic and euvolemic hyponatremia, including patients with heart failure, cirrhosis, and Syndrome of Inappropriate Antidiuretic Hormone (SIADH). In view of the latest FDA's recommendation, the matter will be discussed in the coming meeting of the Registration Committee of the Pharmacy and Poisons Board.

2. Carbamazepine – Recommendations for HLA-B*1502 genotype testing prior to the initiation of treatment in new patients

HSA alerted healthcare professionals that genotyping for the HLA-B*1502 allele prior to the initiation of carbamazepine (CBZ) therapy in new patients of Asian ancestry is now considered the standard of care. HSA will strengthen the local package inserts for this drug product to highly recommend HLA-B*1502 genotyping test.

Please refer to HSA's website for details:

http://www.hsa.gov.sg/publish/hsaportal/en/health_products_regulation/safety_information/DHCPL.html

In Hong Kong, there are twelve registered pharmaceutical products containing carbamazepine. They are prescription-only medicines and indicated for the treatment of epilepsy and other conditions such as trigeminal neuralgia and bipolar disorders. Letter regarding carbamazepine induced Steven Johnson Syndrome and Toxic Epidermal Necrolysis are significantly more common in patients with a particular human leucocyte antigen (HLA) allele HLA-B*1502, which occurs almost exclusively in patients with ancestry across broad areas of Asia was issued on 7 May 2008. In view of HSA's action, the matter will be discussed in the coming meeting of the Registration Committee of the Pharmacy and Poisons Board.

Please encourage your members to report any adverse events caused by the drugs to the Pharmacovigilance Unit of Department of Health (tel. no.: 2319 2920, fax: 2186 9845 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly drug safety digest of drug safety news and information issued by Drug Office.

Yours sincerely,

(Ms. Pamela LI)
for Assistant Director (Drug)