衞生署藥物辦公室
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**DEPARTMENT OF HEALTH**
**DRUG OFFICE**
**DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION**
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BY FAX

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(來函請援引此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

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

Dear Dr. LI,

**FDA: Important changes to the neutropenia monitoring recommendations and treatment algorithm for clozapine**

Your attention is drawn to the US Food and Drug Administration's (FDA) announcement regarding important changes to the neutropenia monitoring recommendations and treatment algorithm for clozapine which is outlined as follows:

- Absolute neutrophil count (ANC) is the only test result accepted in the Clozapine risk evaluation and mitigation strategy (REMS) Program to monitor for neutropenia.
- Patients with benign ethnic neutropenia (BEN) can now be treated with clozapine.
- There are two ANC monitoring algorithms:
  - For general population patients, i.e., those without benign ethnic neutropenia (BEN), interrupt treatment if neutropenia is suspected to be clozapine-induced for ANC less than 1,000 cells per microliter.
  - For patients with BEN, interrupt treatment if neutropenia is suspected to be clozapine-induced for ANC less than 500 cells per microliter.
- Although re-challenging patients who develop severe neutropenia during treatment with clozapine is not recommended, under the revised prescribing information prescribers will have more flexibility to make individualized treatment decisions for their patients if they determine that the risk of psychiatric illness is greater than the risk of recurrent severe neutropenia.

Please refer to the FDA's website for details:

http://www.fda.gov/Drugs/DrugSafety/ucm461853.htm

In Hong Kong, there are 7 registered pharmaceutical products containing clozapine, and all of them are prescription-only medicines. In January and March 2012, the Department of Health (DH) issued letters to the registration certificate holders of the 7 products containing clozapine to remind them of the following registration requirements of their products:

1) the drug should only be supplied to psychiatrists with a prescribing guideline, a letter of undertaking to be signed by the psychiatrists declaring that he/she is familiar with the drug, including the restricted indications and risk of agranulocytosis;

2) patient blood monitoring programme to be implemented before, during, and after the discontinuation of the drug; and

3) patient information leaflet with warnings on the risks of the drug.

So far, DH has received two cases of adverse drug reaction after the use of clozapine, and one of them was related to agranulocytosis.

In view of the US FDA's announcement to enhance the prescribing information and risk management program for clozapine, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 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 digest of drug safety news and information issued by Drug Office.

Yours sincerely,

(Grant NG)
for Assistant Director (Drug)