衞生署藥物辦公室
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DEPARTMENT OF HEALTH
DRUG OFFICE
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(IN REPLY PLEASE QUOTE THIS FILE REF.)

Dear Healthcare Professionals,

PRAC recommends new measures to avoid valproate exposure in pregnancy. New restrictions on use; pregnancy prevention programme to be put in place.

Your attention is drawn to the European Medicines Agency's (EMA) announcement that the EMA Pharmacovigilance Risk Assessment Committee (PRAC) is recommending new measures to avoid exposure of babies to valproate medicines in the womb. Babies exposed are at risk of malformations and developmental problems.

Medicines containing valproate have been approved nationally in the EU to treat epilepsy, bipolar disorder and in some countries for prevention of migraine. They are known to pose a considerable risk of malformations and developmental problems in babies who are exposed to valproate in the womb. An earlier review had recommended measures aimed at better informing women about these risks in order to reduce use of the medicine during pregnancy, and not starting treatment unless other options were ineffective or could not be used because of side effects. The current review was launched because of concerns that these measures had not been sufficiently effective.

The PRAC examined the available evidence and consulted widely with healthcare professionals and with patients, including women and their children who have been affected by valproate use during pregnancy, through written submissions, expert meetings, meetings with stakeholders including healthcare professionals, patients organisations, patients and their families, and via a public hearing. The PRAC noted that women were still not always receiving the right information in a timely manner and that further measures were needed to help avoid use during pregnancy. However, it was also clear that for some women, such as those with particular forms of epilepsy, valproate is the only appropriate treatment and might be life-saving. The PRAC therefore considered that the way the products are used should be changed. It recommended strengthening restrictions on their use and introducing new measures to require appropriate counselling and information for affected women.

The PRAC also recommended that the companies marketing these medicines carry out additional studies to further characterise the nature and extent of the risks posed by valproate and to monitor ongoing valproate use and the long-term effects from affected pregnancies.

The main measures recommended include:

- Where licensed for migraine or bipolar disorder: In pregnancy - valproate must not be used; In female patients from the time they become able to have children - valproate must not be used unless the conditions of a new pregnancy prevention programme are met.
- For epilepsy: In pregnancy - valproate must not be used. However it is recognised that for some women with epilepsy it may not be possible to stop valproate and they may have to continue treatment (with appropriate specialist care) in pregnancy; In female patients from the time they become able to have children - valproate must not be used unless the conditions of the new pregnancy prevention programme are met.
- The PRAC has also recommended that the outer packaging of all valproate medicines must include a visual warning about the risks in pregnancy. In addition to boxed text, this may include a symbol/pictogram, with the details to be adapted at national level.
- A patient reminder card will also be attached to the outer package for pharmacists to discuss with the patient each time the medicine is dispensed. Companies that market valproate should also provide updated educational materials in the form of guides for healthcare professionals and patients.

Please refer to the following website in EMA for details:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/referrals/Valproate_and_related_substances/human_referral_prac_000066.jsp&mid=WC0b01ac05805c516f

In Hong Kong, there are 12 registered pharmaceutical products containing valproic acid and/or valproate, and all products are prescription-only medicines. In Dec 2014, the Registration Committee of the Pharmacy and Poisons Board discussed the findings of an EMA's previous review on the risks of valproate products in pregnancy and had decided that warnings and precautions on the risks of pregnancy should be included in valporate products. So far, the Department of Health (DH) has received 8 cases of adverse drug reaction in connection with valproic acid or valproate, but none of them was related to adverse effects in new-born babies whose mothers took valproate for their medical conditions. As the PRAC new recommendations will now be sent to Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) for further adoption, DH will remain vigilant on the development of the issue and safety update of the drug issued by other overseas drug regulatory authorities. 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 faithfully,

(Joseph LEE)

for Assistant Director (Drug)