Dear Healthcare Professionals,

PRAC recommends modified-release paracetamol be removed from market

Your attention is drawn to the European Medicines Agency’s (EMA) recommendation following a review that modified- or prolonged-release paracetamol products (designed to release paracetamol slowly over a longer period than the usual immediate-release products) should be suspended from marketing. This is in view of the risks to patients from the complex way these medicines release paracetamol into the body after an overdose.

The review of modified-release paracetamol has been carried out by EMA’s Pharmacovigilance Risk Assessment Committee (PRAC), following a request from the Swedish medicines authority, the Medical Products Agency, which had noted problems in managing overdose with such a product since marketing approval. The PRAC evaluated published studies and reports of overdose with these medicines, consulted experts in the management of poisoning and assessed how overdose with paracetamol is managed in the EU and other parts of the world.

Experience has shown that in overdose (particularly at high doses), because of the way the paracetamol in modified-release products is released in the body, the usual treatment procedures developed for immediate-release products are not appropriate. If doctors are not aware modified-release paracetamol has been taken, which affects decisions such as when and for how long to give an antidote, overdose might result in severe liver damage or death. In modified-release products that also contain the painkiller tramadol this could be complicated further because of the additional effects of overdose with tramadol.

In many cases, it may not be known whether an overdose of paracetamol involves immediate-release or modified-release products, making it difficult to decide what type of management is needed. The Committee could not identify means to minimise the risk to patients, or a feasible and standardised way to adapt the management of paracetamol overdose across the European Union (EU) to allow for treatment of cases that involve modified-release preparations. It concluded on balance that the risk following overdose with these medicines outweighs the advantage of having a longer-acting preparation. The Committee therefore recommended that marketing of modified-release paracetamol medicines should be suspended. Immediate-release paracetamol products, which are not affected by this review, will continue to be available as before.

When used appropriately and in recommended doses the benefits of paracetamol outweigh its risks. It remains important that patients seek medical advice quickly if they have taken, or think
they may have taken, more than the recommended amount of any paracetamol-containing product. Patients should also consult a healthcare professional if they have any other concerns about their medication.

Please refer to the following website in EMA for details:


In Hong Kong, there are 7 registered pharmaceutical products containing paracetamol in modified-/prolonged-release dose form and they belong to non-prescription medicines. The 7 products include Clariflu Sustained Release Tab (HK-47205) which is registered by Bayer Healthcare Ltd; Panadol Joint Extended Release Caplet 665mg (HK-59436), Panadol Long Lasting Tab 665mg (HK-51314), Panadol Extend Tab 665mg (HK-51316) and Panadol Extend Tab 665mg (Ireland) (HK-52683) which are registered by GlaxoSmithKline Consumer Healthcare (Hong Kong) Limited; Xykaa Extend Prolonged Release Tablet 650mg (HK-61400) which is registered by Evercare Pharmaceutical Co. Ltd; and Ensid-ER Extended Release Tablet 650mg (HK-62272) which is registered by LSB (HK) Ltd.

So far, the Department of Health (DH) has received 10 adverse drug reaction cases related to overdose/ liver injury after taking paracetamol. In February 2011, the Registration Committee of the Pharmacy and Poisons Board had discussed the risk of liver toxicity related to paracetamol, and decided that the sales packs of paracetamol products should include warnings on the potential risks of liver toxicity and damage, and advice against using more than the recommended dose and against using more than one product containing paracetamol. As the concerned companies in the EU have the rights to request the PRAC to re-examine its recommendations before sending to CMDh and EMA for endorsement, DH will continue to remain vigilant on the development of this issue and safety updates on paracetamol by other overseas health 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)

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