PHARMACY AND POISONS BOARD
HONG KONG
香港藥劑業及毒藥管理局

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衞生署藥物辦公室

29th April 2024

To: Certificate holders of registered pharmaceutical products

Dear Sir/Madam,

New Warnings for Methylphenidate Long-Acting (modified-release) Preparations

On 25th April 2024, the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee (the Committee) considered the latest warnings regarding switching patients between different methylphenidate long-acting (modified-release) preparations by the drug regulatory authorities of Canada, Singapore, the United Kingdom and the United States, and decided that the sales pack labels and / or package inserts of all registered products containing methylphenidate long-acting (modified-release) preparations should include one of the following new safety information (or equivalent [Note 1]) as appropriate:

> *"Switching from Other Methylphenidate Products*
> *Do not substitute for other methylphenidate products on a milligram-per-milligram basis, because of different methylphenidate base compositions and differing pharmacokinetic profiles.",*
>
> *or*

Note 1 Related safety information with other wording in accordance with reputable references and/or approved package inserts from drug regulatory authorities of reference countries may also be accepted on a case-by-case basis.

"Choice of methylphenidate formulation
Caution is advised if long-acting formulations of methylphenidate are used interchangeably due to the differences between these formulations in frequency of dosing, administration with food and plasma drug concentration achieved.",

or

"Changing from one extended-release methylphenidate product to another
The efficacy and tolerability profile of <Product name/Generic name> over the dosing period is determined by the specific release profile of the product. Other extended-release methylphenidate formulations with different release profiles may have different efficacy and tolerability profiles. If changing from one extended-release methylphenidate product to another, it is recommended that this be carried out only with additional medical supervision."

You are therefore required to ensure the sales pack labels and / or package inserts of the concerned products registered by your company contain the above safety information to comply with the new requirements. In addition, you are reminded to ensure the sale pack labels and / or package inserts of the registered methylphenidate products already contain the safety information stated in the Annex (or equivalent [see Note 1 above]) as previously endorsed by the Committee. Please submit application for the change of the registered particular(s) to the Drug Office via the online Pharmaceutical Registration System 2.0 (PRS 2.0) at www.drugoffice.gov.hk/prs2-ext/client_authentication.jsp for approval within 2 months from the date of this letter. Failing to comply with the above requirements may result in de-registration of the products or registration not being renewed by the Committee upon certificate expiry.

For further enquiries on the registration matters of pharmaceutical products, please contact the Drug Office at 3974 4175.

Yours faithfully,

(Y. F. YEUNG)
Secretary,
Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee

c.c. 7-15/3, Product Files

Annex

Safety information previously endorsed by the Pharmacy and Poisons (Registration of Pharmaceutical Substances: Certificate of Clinical Trial/Medicinal Test) Committee

For all methylphenidate-containing pharmaceutical products:

(i) The safety information related to priapism. Example of wording as follows:

*"**Priapism***
Prolonged and painful erections, sometimes requiring surgical intervention, have been reported with methylphenidate use, in both adult and pediatric male patients. Although priapism was not reported with methylphenidate initiation, it developed after some time on methylphenidate, often subsequent to an increase in dosage. Priapism also occured during methylphenidate withdrawal (drug holidays or during discontinuation).

<Product name/Generic name>-treated patients who develop abnormally sustained or frequent and painful erections should seek immediate medical attention."

(ii) The safety information related to suicidal behavior and ideation. Example of wording as follows:

*"**Suicidal Behaviour and Ideation***
There have been post-marketing reports of suicide-related events in patients treated with Attention Deficit Hyperactivity Disorder (ADHD) drugs, including cases of ideation, attempts, and very rarely, completed suicide. The mechanism of this risk is not known. ADHD and its related co-morbidities may be associated with increased risk of suicidal ideation and/or behaviour.

Therefore, it is recommended for patients treated with ADHD drugs that caregivers and physicians monitor for signs of suicide-related behaviour, including at dose initiation/optimization and drug discontinuation. Patients should be encouraged to report any distressing thoughts or feelings at any time to their healthcare professional. Patients with emergent suicidal ideation and behaviour should be evaluated immediately. The physician should initiate appropriate treatment of the underlying psychiatric condition and consider a possible change in the ADHD treatment regimen."

(iii) The safety information related to the use in pregnancy. Example of wording as follows:

*"**Pregnancy***
Data from a cohort study of in total approximately 3,400 pregnancies exposed in the first trimester do not suggest an increased risk of overall birth defects. There was a small increased occurrence of cardiac malformations (pooled adjusted relative risk, 1.3; 95 % CI, 1.0-1.6) corresponding to 3 additional infants born with congenital cardiac malformations for every 1000 women who receive methylphenidate during the first trimester of pregnancy, compared with non-exposed pregnancies.

Cases of neonatal cardio-respiratory toxicity, specifically fetal tachycardia and respiratory distress have been reported in spontaneous case reports.

Studies in animals have only shown evidence of reproductive toxicity at maternally toxic doses.

Methylphenidate is not recommended for use during pregnancy unless a clinical decision is made that postponing treatment may pose a greater risk to the pregnancy."