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

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1st March 2022

To: Certificate holders of
registered pharmaceutical products

Dear Sir / Madam,

New Warnings for Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

On 21st February 2022, the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee (the Committee) considered the latest new warnings on the use of pharmaceutical products containing NSAIDs (examples are provided in Annex) at 20 weeks gestation or later in pregnancy and the risk of fetal kidney problems by the drug regulatory authorities of Australia, Canada, the European Union, Singapore, the United Kingdom and the United States, and decided that the sales pack labels and / or package inserts of registered pharmaceutical products containing NSAIDs for human use (excluding products which contain aspirin 81mg or below, products administered directly to the eye or ear, or those indicated for children only) should include the following new safety information (or equivalent) as appropriate:

"Warnings and Precautions

Special Populations

Pregnant Women: [Product Name / Generic Name] are contraindicated for use during the third trimester of pregnancy because of risks of premature closure of the ductus arteriosus and the potential to prolong parturition. Caution is recommended in prescribing [Product Name / Generic Name] during the first and second trimesters of pregnancy, particularly from the middle to end of the second trimester of pregnancy (onset at approximately 20 weeks) due to possible fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment or failure.

[Product Name / Generic Name] should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus.

Published studies and postmarketing reports describe maternal Non-Steroidal Anti-Inflammatory Drug (NSAID) use at approximately 20 weeks gestation or later in pregnancy associated with fetal renal dysfunction leading to oligohydramnios, and in some cases, neonatal renal impairment or failure. NSAIDs were shown to cause significant reduction in fetal urine production prior to reduction of amniotic fluid volume. There have also been a limited number of case reports of maternal NSAID use and neonatal renal dysfunction and renal impairment without oligohydramnios, some of which were irreversible, even after treatment discontinuation.

These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation.

Complications of prolonged oligohydramnios may for example, include limb contractures and delayed lung maturation. In some postmarketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required.

If after careful consideration of the benefit-risk, NSAID treatment is considered necessary to be administered anywhere from the middle (onset at approximately 20 weeks) to the end of the second trimester of pregnancy, the use should be limited to the lowest effective dose and shortest duration possible. It is also recommended that ultrasound monitoring of amniotic fluid be considered if [Product Name / Generic Name] treatment extends

beyond 48 hours and that NSAIDs treatment be discontinued if oligohydramnios occurs, followed by appropriate medical follow up.

Contraindications

The third trimester of pregnancy, because of risks of premature closure of the ductus arteriosus, and prolonged parturition."

You are therefore required to review and revise, if necessary, the sales pack labels and / or package inserts of the concerned products registered by your company to ensure that the products comply with the above new requirements. The revised sales pack labels and / or package inserts should be submitted to the Committee 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 renewed by the Committee.

If you have any enquiries on the above issue, please contact Ms. Queenie CHAN at 3974 4147.

Yours faithfully,

(T.K. YIM)
Secretary,
Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee

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

TK/QC

Annex

Examples of NSAIDs

Acemetacin, aspirin, celecoxib, dexketoprofen, diclofenac, etodolac, etofenamate, etoricoxib, felbinac, flurbiprofen, ibuprofen, indomethacin, ketoprofen, ketorolac, mefenamic acid, meloxicam, naproxen, nimesulide, parecoxib, phenazone, piroxicam, proglumetacin, propyphenazone, sulindac and tenoxicam, etc.