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Dear Healthcare Professionals,

FDA recommends avoiding use of NSAIDs in pregnancy at 20 weeks or later because they can result in low amniotic fluid

Your attention is drawn to the United States Food and Drug Administration's (FDA) warning that use of nonsteroidal anti-inflammatory drugs (NSAIDs) around 20 weeks or later in pregnancy may cause rare but serious kidney problems in an unborn baby. This can lead to low levels of amniotic fluid surrounding the baby and possible complications. NSAIDs are commonly used to relieve pain and reduce fevers. They include medicines such as aspirin, ibuprofen, naproxen, diclofenac, and celecoxib. After around 20 weeks of pregnancy, the unborn babies' kidneys produce most of the amniotic fluid, so kidney problems can lead to low levels of this fluid. Amniotic fluid provides a protective cushion and helps the unborn babies' lungs, digestive system, and muscles develop.

Although this safety concern is well known among certain medical specialties, FDA wanted to communicate its recommendations more widely to educate other health care professionals and pregnant women. This issue affects all NSAIDs that are available by prescription and those that can be bought over-the-counter (OTC) without a prescription.

For prescription NSAIDs, FDA is requiring changes to the prescribing information to describe the risk of kidney problems in unborn babies that result in low amniotic fluid. FDA is recommending avoiding NSAIDs in pregnant women at 20 weeks or later in pregnancy rather than the 30 weeks currently described in NSAID prescribing information. At around 30 weeks, NSAIDs can cause a problem that may result in heart issues in the unborn baby. If deemed necessary by a health care professional, use of NSAIDs between 20 and 30 weeks of pregnancy should be limited to the lowest effective dose for the shortest duration. The changes to the prescribing information also indicate that health care professionals should consider ultrasound monitoring of amniotic fluid if NSAID treatment extends beyond 48 hours.

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aspire to be an internationally renowned public health authority*

FDA will also update the Drug Facts labels of OTC NSAIDs intended for use in adults. These labels already warn to avoid using NSAIDs during the last 3 months of pregnancy because the medicines may cause problems in the unborn child or complications during delivery. The Drug Facts labels already advise pregnant and breastfeeding women to ask a health care professional before using these medicines.

One exception to the above recommendations is the use of the low 81 mg dose of the NSAID aspirin for certain pregnancy-related conditions at any point in pregnancy under the direction of a health care professional.

FDA reviewed the medical literature and cases reported to FDA for data about low amniotic fluid levels or kidney problems in unborn babies associated with NSAID use during pregnancy. Among the 35 cases of low amniotic fluid levels or kidney problems reported to FDA through 2017, all were serious. This number includes only cases submitted to FDA, so there may be additional cases. Two newborns who died had kidney failure and confirmed low amniotic fluid when mothers took NSAIDs while pregnant; three other newborns who died had kidney failure without confirmed low amniotic fluid when mothers took NSAIDs while pregnant. The low amniotic fluid levels started as early as 20 weeks of pregnancy. In 11 cases where low amniotic fluid levels were detected during pregnancy, the fluid volume returned to normal after the NSAID was stopped. The information from the cases was similar to what was found in the medical literature. In these publications, low amniotic fluid levels were detected with use of NSAIDs for varying amounts of time, ranging from 48 hours to multiple weeks. In most cases, the condition was reversible within 3 to 6 days after stopping the NSAID. In many reports, the condition was reversed when the NSAID was stopped, and it reappeared when the same NSAID was started again.

Please refer to the following website in FDA for details:

<https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-avoiding-use-nsaids-pregnancy-20-weeks-or-later-because-they-can-result-low-amniotic>

In Hong Kong, there are registered pharmaceutical products containing nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, naproxen, diclofenac and celecoxib. So far, the Department of Health (DH) has received adverse drug reaction related to aspirin (49 cases) and other NSAIDs (38 cases), but these cases are not related to low levels of amniotic fluid. In light of the above FDA's announcement, 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 Undesirable Medical Advertisements and Adverse Drug Reaction 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)