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(來函請敍明此檔案號碼) DH DO DIMC/7-30/1
(IN REPLY PLEASE QUOTE THIS FILE REF.)

31 Mar 2022

Dear Healthcare Professionals,

FDA recommends thyroid monitoring in babies and young children who receive injections of iodine-containing contrast media for medical imaging

Your attention is drawn to the United States Food and Drug Administration's (FDA) announcement that newborns and children through 3 years old are recommended to have follow-up thyroid monitoring within 3 weeks after receiving injections of contrast media containing iodine for X-rays and other medical imaging procedures, based on its recent review of published studies. FDA's review showed that underactive thyroid or a temporary decrease in thyroid hormone levels were uncommon. However, the conditions should be identified and treated early when needed to prevent potential future complications. Newborns, particularly those born premature, and children in their first 3 years with underlying conditions such as heart issues may be at higher risk for problems of the thyroid.

FDA has approved a new warning to the prescribing information for the entire class of iodinated contrast media (ICM) injections and monitoring recommendations for children 3 years or younger. The warning describes the risk of underactive thyroid or a temporary decrease in thyroid hormone levels. These risks and recommendations pertain to ICM given as an injection through an artery or vein.

Since 2015 when FDA first alerted the public about cases of underactive thyroid in infants receiving ICM, six new research studies evaluating this risk have been published. FDA reviewed these six studies and the five earlier ones published in the medical literature that assessed thyroid function in a range of 10 to 2,320 children from birth through 3 years who were exposed to ICM. Most cases of decreased thyroid hormone levels were temporary and did not require treatment. The reported rate ranged from 1 percent to 15 percent and tended to be higher in newborns, particularly those who were preterm. Patients with cardiac conditions were at greatest risk since they often require high doses of contrast during invasive cardiac procedures such as catheterization and computed tomography. The time from ICM exposure to diagnosis ranged between 8.5 and 138 days, with most occurring within 3 weeks in some of the publications.

In 2015, FDA required the manufacturers of ICM products to conduct a study to investigate this safety issue further. However, FDA has concluded based on its review of the published studies that there is compelling evidence of a significant risk for underactive thyroid or a temporary decrease in thyroid hormone levels in newborns and children through 3 years after exposure to ICM. Therefore, the study by the manufacturers is no longer needed.

Health care professionals should perform appropriate monitoring of patients from birth through 3 years for the possibility of hypothyroidism or a temporary decrease in thyroid hormone levels following exposure to ICM. Consider evaluating thyroid function within 3 weeks, especially in term and preterm neonates and children with some underlying conditions. If thyroid dysfunction is detected, treat and monitor thyroid function as clinically needed to avoid future cognitive and other developmental disabilities. Certain pediatric patients are at an increased risk, including those who are newborns or have very low birth weight, prematurity, or the presence of cardiac or other conditions such as those requiring care in neonatal or pediatric intensive care units. Patients with cardiac conditions may be at greatest risk since they often require high doses of contrast during invasive cardiac procedures.

Please refer to the following website in FDA for details:
https://www.fda.gov/drugs/drug-safety-and-availability/fda-recommends-thyroid-monitoring-babies-and-young-children-who-receive-injections-iodine-containing

In Hong Kong, there are registered pharmaceutical products which are iodine-containing contrast agents containing iodixanol (2 products), iohexol (2 products), iopamidol (2 products), iopromide (2 products), ioversol (4 products), iomeprol (4 products), iobitridol (6 products) and iodised oil (1 product). All products are prescription-only medicines. So far, the Department of Health (DH) has received adverse drug reaction related to iodixanol (3 cases), iohexol (1 case), iopamidol (3 cases), iopromide (7 cases), iobitridol (4 cases) and iodised oil (2 cases), but these cases were not related to decreased thyroid function. The DH has not received any case of adverse drug reaction related to ioversol and iomeprol.

Related news was previously issued by various overseas drug regulatory authorities, and was posted on the Drug Office website since 18 Nov 2015, with the latest update posted on 19 Sep 2018. Letters to inform local healthcare professionals were issued by the DH on 18 Nov 2015. In Apr 2016, the Registration Committee of the Pharmacy and Poisons Board discussed the matter and decided that the sales pack labels and/or package inserts of iodine-containing contrast agents should include safety warnings on the risk of hypothyroidism. In light of the above FDA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is

not intended to serve as guidelines or to replace professional clinical judgement. 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 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,

pp (Terence MAN)
for Assistant Director (Drug)