



Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION



FDA ADVISORY
No. **2019-328**

07 OCT 2019

TO: ALL HEALTHCARE PROFESSIONALS AND MARKET AUTHORIZATION HOLDERS

SUBJECT: Safety Information: Risk of Non-melanoma skin cancer with prolonged use of hydrochlorothiazide

Introduction

Singapore has released an update to healthcare professionals on two recent pharmacoepidemiological studies using data from Danish registries which suggested a cumulative dose-dependent association between the prolonged use of hydrochlorothiazide-containing medicines and Non-melanoma skin cancer (NMSC).

Scientific Discussion

Hydrochlorothiazide (HCTZ) is used alone or together with other medicines to treat high blood pressure (hypertension). It is also used to treat fluid retention (edema) that is caused by congestive heart failure, severe liver disease (cirrhosis), kidney disease, or treatment with a steroid or hormone medicine.

Skin cancer is one of the most common cancers worldwide. It used to be more common among caucasians, but with the depletion of the ozone layer, ultraviolet rays from the sun are now capable of causing skin cancer. Other factors that cause skin cancer include: exposure to coal, arsenic, genetics, and pre-existing skin conditions, immunosuppression and photosensitizing medications. Skin cancer has two major types: Melanoma and Non-melanoma skin cancer (NMSC). NMSC has two subtypes: Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC). Both are commonly seen on older generation because 80% of these tumors is caused by cumulative sun exposure.

There are about 302 HCTZ prescription drugs that have been registered in the Philippines, either as single ingredient or fixed-dose combinations. To date, FDA Philippines has not received any adverse drug reactions reports of Non-melanoma skin cancer with prolonged use of HCTZ.

Safety Advisory

Healthcare professionals should inform their patients on the risk of NMSC and should advise them to regularly check their skin for new marks or growths and any changes to existing marks. Alternatives to HCTZ may be considered for patients who are at high risk for NMSC such as known personal or family history of skin cancer, ongoing immunosuppressive therapy and light colored skin. Possible preventive measures such as limited exposure to sunlight and UV rays



and, in case of exposure, adequate protection should be advised to the patients in order to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies.

Healthcare professionals are also encouraged to report any serious adverse reactions, including Non-melanoma skin cancer, related to HCTZ-containing products, to the FDA.

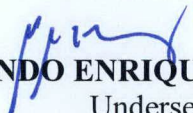
Information for Market Authorization Holders

The Market Authorization Holders of HCTZ-containing products shall update their respective package inserts to reflect the information on risk of Non-melanoma skin cancer. This information should appear under Special Warnings and Precautions. MAHs are hereby directed to submit their revised package inserts in relation to the above safety concern by filing variation application within 3 months after this issuance.

Provided below is the suggested text for the revised package insert:

An increased risk of non-melanoma skin cancer (NMSC) [basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)] with increasing cumulative dose of hydrochlorothiazide (HCTZ) exposure has been observed in two epidemiological studies based on the Danish National Cancer Registry. Photosensitizing actions of HCTZ could act as a possible mechanism for NMSC.

Patients taking HCTZ should be informed of the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Possible preventive measures such as limited exposure to sunlight and UV rays and, in case of exposure, adequate protection should be advised to the patients in order to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. The use of HCTZ may also need to be reconsidered in patients who have experienced previous NMSC.


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Safety Information:

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