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### IN BRIEF

#### Hydrochlorothiazide and Skin Cancer

The FDA has required the addition of information about an increased risk of nonmelanoma skin cancer (basal cell carcinoma [BCC] and squamous cell carcinoma [SCC]) to the labels of products containing the diuretic hydrochlorothiazide.<sup>1</sup>

The labeling change was based on a review of published observational studies and on the results of an observational study conducted in the FDA's Sentinel system. In a national case-control study in Denmark, use of hydrochlorothiazide was associated with an increased risk of BCC and SCC (adjusted odds ratio [OR] 1.08 for BCC and 1.75 for SCC). The increase in risk correlated with the cumulative dose of the drug; among patients who received a lifetime hydrochlorothiazide dose of  $\geq 50,000$  mg (equivalent to 25 mg/day for  $\sim 5.5$  years), the adjusted OR was 1.29 for BCC and 3.98 for SCC compared to those who had never taken the drug.<sup>2</sup>

In the FDA Sentinel Study, 5.2 million new users of hydrochlorothiazide were matched with an equal number of new users of an angiotensin-converting enzyme (ACE) inhibitor. The use of hydrochlorothiazide was associated with an increased risk of SCC of about 1 case per 16,000 treated patients per year. This increase in risk correlated with the cumulative hydrochlorothiazide dose; it was statistically signi-

ficant in white patients ( $\sim 1$  additional case per 7000 patient-years), but not in nonwhite subgroups.<sup>3</sup>

Given the significant risks of uncontrolled blood pressure and the very small absolute risk of nonmelanoma skin cancer associated with use of hydrochlorothiazide, patients should generally be encouraged to continue taking the drug. Indapamide, a long-acting thiazide-like diuretic, was associated with an increased risk of malignant melanoma in one case-control study in Denmark.<sup>4</sup> Whether the long-acting thiazide-like diuretic chlorthalidone increases the risk of skin cancer has not been determined. Patients taking any thiazide or thiazide-like diuretic should have regular skin cancer screenings and limit their UV radiation exposure.<sup>5</sup> ■

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3. E Eworuke et al. Risk of non-melanoma skin cancer associated with hydrochlorothiazide-containing products in the United States. International Conference on Pharmacoepidemiology & Therapeutic Risk Management. Virtual event. September 16-17, 2020. Available at: <https://bit.ly/3eqHHQy>. Accessed November 5, 2020.
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