Asians on Phenytoin at High Skin Reaction Risk

BY ELIZABETH MECHCATIE
Senior Writer

The Food and Drug Administration is investigating preliminary data indicating that people who have the human leukocyte antigen allele HLA-B*1052 may be at a greater risk of developing Stevens-Johnson syndrome and toxic epidermal necrolysis during treatment with phenytoin or fosphenytoin.

The allele is found "almost exclusively in patients with ancestry across broad areas of Asia, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and Thais," the FDA announced in a posting on the agency's MedWatch site in November.

Until the FDA completes the evaluation, "health care providers should consider avoiding phenytoin and fosphenytoin as alternatives for carbamazepine in patients who test positive for HLA-B*1502,"

Until the evaluation has been completed, 'providers should consider avoiding phenytoin and fosphenytoin as alternatives for carbamazepine in patients who test positive for HLA-B*1502.'

the FDA advised.

In December 2007, the FDA announced that people of Asian ancestry with the same allele who were taking carbamazepine were at an increased risk of Stevens-Johnson syndrome (SJS) and and toxic epidermal necrolysis (TEN).

The label for carbamazepine now reads that testing for the allele is recommended when considering using carbamazepine in a patient who fits any of the categories, and that if it is present, it should not be used "unless the benefits clearly outweigh the risks," according to the FDA.

However, because the potential risks associated with phenytoin and fosphenytoin still are being investigated, "there is not yet enough information to recommend testing" for the allele in patients of Asian ancestry being considered for treatment with one of these two antiepileptic drugs.

An estimated 10%-15% of people in parts of China, Thailand, Malaysia, Indonesia, the Philippines, and Taiwan may have this allele.

An average 2%-4% of South Asians, including Indians, "appear" to have the allele, but the rate may be higher in some groups, according to the statement from the agency.

The frequency of the allele appears to be low—less than 1%—among people in Japan and Korea.

The risk of serious skin reactions with these two drugs appears to be at its highest during the first months of treatment, which is also true for carbamazepine. More than 90% of people who have had a skin reaction with carbamazepine had it during the first months of treatment, whereas people who have been treated with the drug for a longer period "are at low risk of developing this reaction," according to the FDA.

Phenytoin is marketed as Dilantin, Phenytex, and in generic formulations as well. Fosphenytoin, marketed as Cerebyx and also in generic formulations, is a prodrug of phenytoin.

The FDA is analyzing data from a study that reported that four of four Thai patients who developed SJS during treatment with phenytoin had the HLA-B*1502 allele.

However, only 18% of a control group of people who were able to tolerate phenytoin tested positive for the allele (Epilepsia 2008;49:2087-91).

The FDA said in its statement that it plans to provide updates on this issue as more information becomes available. ■

A link to the notice as well as related information is available at www.fda.gov/medwatch/safety/2008/safety08.htm#Phenytoin.

Serious or unexpected adverse events associated with these drugs can be reported to MedWatch at 800-332-1088 or www.fda.gov/medwatch/report.htm.