

**Test:** Carbamazepine Sensitivity Genotyping (HLA B 15020)

**Date:** November 3, 2008

**Test Overview:**

The FDA issued an alert on 12/12/07 recommending pre-therapy genetic screening for the presence of the HLA-B\*1502 allele for patients with ancestry from Asia, including South Asian Indians. If these patients test positive, carbamazepine should not be started unless the expected benefit clearly outweighs the risk of serious skin reactions (Stevens Johnson syndrome and toxic epidermal necrolysis). This test does not discriminate between HLA-B\*1502, HLA-B\*9512 or other rare alleles. Confirmation by sequence is available upon request.

**Clinical Significance:**

Serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), have been reported with Carbamazepine treatment. The risk of these events is estimated to be about 1 to 6 per 10,000 new users in countries with mainly Caucasian populations. However, the risk in some Asian countries is estimated to be about 10 times higher. Carbamazepine should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest SJS/TEN, use of this drug should not be resumed and alternative therapy should be considered.

Retrospective case-control studies have found that in patients of Chinese ancestry there is a strong association between the risk of developing SJS/TEN with carbamazepine treatment and the presence of an inherited variant of the HLA-B gene, HLA-B\*1502. The occurrence of higher rates of these reactions in countries with higher frequencies of this allele suggests that the risk may be increased in allele-positive individuals of any ethnicity. Across Asian populations, notable variation exists in the prevalence of HLA-B\*1502. Greater than 15% of the population is reported positive in Hong Kong, Thailand, Malaysia, and parts of the Philippines, compared to about 10% in Taiwan and 4% in North China. South Asians, including Indians, appear to have intermediate prevalence of HLA-B\*1502, averaging 2 to 4%, but higher in some groups. HLA-B\*1502 is present in <1% of the population in Japan and Korea. HLA-B\*1502 is largely absent in individuals not of Asian origin (e.g., Caucasians, African-Americans, Hispanics, and Native Americans).

In deciding which patients to screen, the rates provided above for the prevalence of HLA-B\*1502 may offer a rough guide, keeping in mind the limitations of these figures due to wide variability in rates even within ethnic groups, the difficulty in ascertaining ethnic ancestry, and the likelihood of mixed ancestry. Carbamazepine should not be used in patients positive for HLA-B\*1502 unless the benefits clearly outweigh the risks. Tested patients who are found to be negative for the allele are thought to have a low risk of SJS/TEN.

Over 90% of Carbamazepine treated patients who will experience SJS/TEN have this reaction within the first few months of treatment. This information may be taken into consideration in determining the need for screening of genetically at-risk patients currently on Carbamazepine. The HLA-B\*1502 allele has not been found to predict risk of less severe adverse cutaneous reactions from Carbamazepine, such as anticonvulsant hypersensitivity syndrome or non-serious rash (maculopapular eruption [MPE]).

Limited evidence suggests that HLA-B\*1502 may be a risk factor for the development of SJS/TEN in patients of Chinese ancestry taking other anti-epileptic drugs associated with SJS/TEN. Consideration should be given to avoiding use of other drugs associated with SJS/TEN in HLAB\* 1502 positive patients, when alternative therapies are otherwise equally acceptable. Application of HLA-B\*1502 genotyping as a screening tool has important limitations and must never substitute for appropriate clinical vigilance and patient management. Many HLA-B\*1502-positive Asian patients treated with Carbamazepine will not develop SJS/TEN, and these reactions can still occur infrequently in HLA-B\*1502-negative patients of any ethnicity. The role of other possible

factors in the development of, and morbidity from, SJS/TEN, such as antiepileptic drug (AED) dose, compliance, concomitant medications, co-morbidities, and the level of dermatologic monitoring have not been studied.

Reference: This information was taken directly from  
<http://www.fda.gov/cder/foi/label/2007/016608s098lbl.pdf>

**Method:**

DNA Amplification and liquid bead array detection.

**Availability:**

Monday-Friday; Results in 7 days.

**Specimen:**

Whole Blood

**Collect:**

10 mL ACD (Yellow) tube. Solution A or B acceptable. Transport to laboratory within 48 hours of collection.

**Volume: 1**

10 mL whole blood

**Transport:**

Room Temperature

**Unacceptable Conditions:**

Heparin tube

**Reference Range:**

With report

**CPT Codes:**

83890; 83898; 83894; 88384; 83912

**Additional Information:**

Client list fee: \$275