HLA-B*15:02 Genotyping, Carbamazepine Hypersensitivity
ARUP test code 2012049

**Positive**

Result: Positive for HLA-B*15:02 allele

Interpretation: The HLA-B*15:02 allele associated with carbamazepine (CBZ) hypersensitivity was detected. The presence of this allele increases risk for CBZ-induced Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) in individuals of Asian ancestry. Patients positive for this allele should not be treated with CBZ, unless the benefits clearly outweigh the risk. Therapy should be discontinued immediately if symptoms of SJS or TEN develop. Alternative medication should be used as first line therapy. Consideration in the choice for alternative medications should be given to potential cross-reactivity with structurally similar aromatic antiepileptic drugs such as oxcarbazepine, phenytoin, fosphenytoin and lamotrigine, which can also moderately increase risk for SJS/TEN in association with HLA-B*15:02 positivity. Performed at: UUHC: Histocompatibility and Immunogenetics, 417 Wakara Way, Ste. 3220, SLC, UT 84108

H=High, L=Low, *=Abnormal, C=Critical
BACKGROUND INFORMATION: HLA-B*1502 Genotype, Carbamazepine Hypersensitivity

CHARACTERISTICS: Carbamazepine (CBZ) is an aromatic antiepileptic drug, approved for the treatment of epilepsy and trigeminal neuralgia. Rarely, CBZ can induce severe life threatening reactions such as Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN). Symptoms usually appear within the first months of treatment, and include skin rash, hives, sores in the mouth, blistering or peeling of the skin, and erosion of the mucous membranes in the respiratory and gastrointestinal tract. The presence of HLA-B*15:02 increases risk for CBZ-induced SJS/TEN in individuals of Asian ancestry. The incidence of CBZ-induced life-threatening reactions such SJS, TEN, or hypersensitivity syndrome (HSS) is 1-10 per 10,000, which can be higher in some Asian countries.

INCIDENCE: HLA-B*15:02 allele frequency varies by ethnicity, with highest incidence in Asians: 10.2 percent in Han Chinese, 10 percent in Taiwanese (18 percent in indigenous Puyuma), greater than 5 percent in the populations of Hong Kong, Thailand, Malaysia, Vietnam, Philippines, India (Khandesh and West Bhil) and Indonesia. Frequency is low in African Americans (0.1-1 percent) and less than 0.1 percent in Caucasians.

INHERITANCE: Autosomal dominant.

CAUSE: In patients of Asian descent, CBZ-induced SJS/TEN is strongly associated with the presence of HLA-B*15:02 allele. The mechanism is immune mediated and involves drug-induced changes in peptide presentation by HLA-B*15:02, which allows for the activation of self-reactive T lymphocytes. Activated immune cells contribute to the cellular death of keratinocytes in the skin, which causes the epidermal destruction and detachment of the skin seen in SJS/TEN.

ALLELES TESTED: HLA-B*15:02 allele. Other members of the HLA-B75 serogroup detected by this assay can also be associated with carbamazepine-induced SJS/TEN, including HLA-B*15:08, 15:11, 15:21, and possibly 15:31 and 15:32.

CLINICAL SENSITIVITY AND SPECIFICITY: 80-97 percent and 99 percent, respectively in populations where the HLA-B*15:02 allele is common.

METHODOLOGY: PCR followed by Sequence Specific Oligonucleotide Probe Hybridization of HLA-B locus.

ANALYTICAL SENSITIVITY AND SPECIFICITY: Greater than 99 percent.

LIMITATIONS: Copy number of HLA-B*15:02 allele will not be reported. Other genetic and non-genetic factors that influence carbamazepine hypersensitivity are not evaluated. Other rare, undocumented alleles may occur which may or may not give false positive results.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS
**VERIFIED/REPORTED DATES**

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