Useful For
- Predicting increased risk of hypersensitivity reactions to allopurinol
- Excluding patients at an elevated risk for allopurinol hypersensitivity syndrome from receiving allopurinol

Clinical Information
Allopurinol is widely used for hyperuricemia-related diseases such as gout, Lesch-Nyhan syndrome, and recurrent urate kidney stones. Allopurinol hypersensitivity syndrome is a spectrum of reactions that includes not only Stevens-Johnson syndrome and toxic epidermal necrolysis, but also systemic disease with a clinical constellation of features such as eosinophilia, vasculitis, rash, and major end-organ disease. There is a reported mortality rate of 20% to 25% for allopurinol hypersensitivity syndrome (AHS).

Studies in Han Chinese residing in Taiwan showed that the HLA-B*5801 allele was present in 100% of the patients with allopurinol-induced skin reactions, but in only 15% of allopurinol-tolerant controls. Data obtained from recombinant mapping further concluded that HLA-B*5801 itself is the major susceptibility gene for allopurinol-induced skin reactions in the Han Chinese population. In the Thai population, 100% of patients with allopurinol-induced skin reactions carried the allele, but only 13% of allopurinol-tolerant individuals tested positive for the HLA-B*5801 allele. A similar but more modest 80% of Korean cases compared to 12% of healthy controls and 56% of Japanese cases compared to 0.61% of healthy controls were positive for the HLA-B*5801 allele. Two studies of Europeans have been reported. In the first study, 55% of European cases compared to 1.5% of controls tested positive for the allele and, in the second study, 100% of cases compared to a population frequency of 1.5% were positive for the HLA-B*5801 allele. A meta-analysis that considered all published studies as of the date of the analysis gave the odds ratios for allopurinol-induced severe skin reactions in HLA-B*5801 carriers as 73 and 165 compared to healthy controls and allopurinol-tolerant controls, respectively. The frequency of the HLA-B*5801 allele is widely distributed among other populations: (eg 2%-4% in Africans, 3%-15% in Asian Indians). Further studies are needed to determine if individuals from these populations with this allele are at similar risk for allopurinol hypersensitivity reaction.

Guidelines have been developed by the Clinical Pharmacogenomics Implementation Consortium that recommend that HLA-B*5801 genotyping be performed and that allopurinol should not be prescribed to patients who test positive for the allele. Also, guidelines developed by the 2012 American College of Rheumatology for Management of Gout recommend that HLA-B*5801 testing should be considered in...
select patient subpopulations at an elevated risk for AHS. Those of Korean descent, especially those with stage 3 or higher chronic kidney disease, or of Han Chinese or Thai extraction, irrespective of renal function, should be tested. However, given the literature as reviewed above, consideration should be given to testing all patients who will be given allopurinol.

**Interpretation**
Positivity for *HLA-B*5801 confers risk for hypersensitivity to allopurinol.

**Cautions**
Rare, unreported *HLA-B58* alleles may occur and may or may not interfere with this assay. This assay also detects closely related, but rare, alleles including *HLA-B*5705, *5804, *5805, *5809, *5810, *5811, *5812, *5813, *5815, *5817, *5819, *5821, *5822, *5823, *5824 and *5828. There are, as yet, no data indicating whether these subtypes are associated with hypersensitivity.

This saliva-based test is especially useful for establishing the *HLA-B*5801 genotype in patients who received a heterologous blood transfusion in the preceding 45 days (6 weeks) or allogeneic bone marrow transplants.

**Reference Values**
An interpretive report will be provided.

**Analytic Time**
1 day

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**Clinical References**

