HLA-B*5701 Genotyping for Abacavir Hypersensitivity

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

<table>
<thead>
<tr>
<th>Procedure addressed by this guideline</th>
<th>Procedure code</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-B*5701 Genotyping</td>
<td>81381</td>
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</tbody>
</table>

What is HLA-B*5701

Definition

Abacavir is used in the treatment of patients with human immunodeficiency virus (HIV).

- The most important adverse effect limiting the use of abacavir is a hypersensitivity reaction (HSR) which occurs in approximately 5-8% of patients.\(^1\)
  - The abacavir HSR includes a combination of rash, fever, GI symptoms (such as nausea, vomiting, diarrhea, or abdominal cramping), constitutional symptoms (tachycardia, hypotension, myalgia, fatigue, pain, malaise, dizziness and headache) and respiratory symptoms.\(^1\)
  - Symptoms usually appear within the first six weeks of abacavir therapy, but can happen at any time.\(^1-3\)

- People with a positive HLA-B*5701 test are at risk for abacavir HSR. Not all HLA-B*5701 carriers will have immunologic-confirmed HSR.\(^2\) In studies of people who have experienced an immunologically-confirmed HSR, about half (47.9%) test positive for the HLA-B*5701 allele.\(^1\)

- People with a negative HLA-B*5701 are at low risk for abacavir HSR. A negative HLA-B*5701 test result does not completely rule out the possibility of an HSR. Those who test negative should be monitored carefully for signs of toxicity, especially in the first six weeks of treatment.\(^4\)

- Demographic risk factors for abacavir HSR show a higher risk in white and Hispanic populations (5-8%) compared to 2-3% in the black population.\(^4,5\) The frequency in Asian populations is very low.\(^2\)

- Screening HIV-1 patients for HLA-B*5701 prior to starting abacavir can reduce the rate of clinically suspected HSR by approximately 60%.\(^1\)
Test information

- HLA-B*5701 testing is performed on a blood or cheek swab sample. The test can be performed in different ways by different labs. Some labs will test for specific gene variants associated with the B*5701 haplotype, where other labs may sequence the DNA in the HLA-B region.

- In general, results can be interpreted as:
  - HLA-B*5701 positive – person is at high risk for developing abacavir HSR; abacavir-containing drugs should be avoided.
  - HLA-B*5701 negative – person is at lower risk for developing abacavir HSR; if abacavir treatment is used, this person should be monitored for toxicity.

Guidelines and evidence

- The Infectious Disease Society of America (2013)\(^6\) and the Department of Health and Human Services’ (DHHS) Panel on Antiretroviral Guidelines for Adults and Adolescents (2016)\(^4\) HIV guidelines recommend that:
  - HLA-B*5701 genotyping should be performed in all patients prior to initiating abacavir therapy.
  - HLA-B*5701 positive patients should not be prescribed abacavir; however, the guidelines state that if abacavir is used in HLA-B*5701 positive patients, careful monitoring for HSR is warranted.
  - A negative test result does not rule out the possibility of an HSR but makes the chance of HSR less likely.
  - Patients should be counseled about the potential for experiencing HSR before being treated with abacavir-containing drugs, regardless of HLA-B*5701 test results.
  - HLA-B*5701 positive status should be recorded as an abacavir allergy in the patient’s medical record.

- The DHHS’s Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children (2016) recommends against the use of abacavir in children who test positive for HLA-B*5701.\(^7\)

- The Clinical Pharmacogenetics Implementation Consortium (CPIC, 2014) published an update to their Guidelines on HLA-B Genotype and Abacavir Dosing.\(^8\) A focused literature review found no new evidence to change their original (2012) recommendations, which include:
  - “HLA-B*5701 screening should be performed in all abacavir-naive individuals before initiation of abacavir-containing therapy.”
"In abacavir-naive individuals who are HLA-B*5701-positive, abacavir is not recommended and should be considered only under exceptional circumstances when the potential benefit, based on resistance patterns and treatment history, outweighs the risk."

"There is some debate among clinicians regarding whether HLA-B*5701 testing is necessary in patients who had previously tolerated abacavir chronically, discontinued its use for reasons other than HSR, and are now planning to resume abacavir. The presence of HLA-B*5701 has a positive predictive value of ~50% for immunologically confirmed hypersensitivity, indicating that some HLA-B*5701-positive individuals can be, and have been, safely treated with abacavir. However, we were unable to find any data to show that HLA-B*5701-positive individuals with previous, safe exposure to abacavir had zero risk of HSR upon re-exposure."

- Product labeling for abacavir-containing drugs recommends:9-11
  - HLA-B*5701 testing prior to initiating treatment with abacavir and prior to reinitiating abacavir when HLA-B*5701 status is unknown even if the patient has previously tolerated treatment with abacavir.
  - For HLA-B*5701-positive patients, treatment with an abacavir-containing regimen is not recommended and should be considered only with close medical supervision and under exceptional circumstances when the potential benefit outweighs the risk.
  - Abacavir is contraindicated in patients with previous hypersensitivity to abacavir.
  - Discontinue abacavir at the first sign of a suspected hypersensitivity reaction.

- Careful monitoring for adverse effects is recommended during the first six weeks of abacavir therapy, when an HSR is most likely to happen. However, an HSR can occur at any time during treatment with abacavir.1,2,9-11

Criteria
HLA-B*5701 testing is indicated in individuals with HIV-1 prior to the initiation of any abacavir-containing therapy.

References
3. Ziagen Prescribing Information. GlaxoSmithKline, Research Triangle Park, NC. May 2018. Available at:


