Statin Sensitivity *SLCO1B1*, 1 Variant

Indications for Ordering

Identify individuals at increased risk for statin-related muscle toxicity

Test Description

Polymerase chain reaction and fluorescence monitoring
- Analyzes variant *SLCO1B1*5* (rs4149056, c.521T>C)

Tests to Consider

Primary test

Statin Sensitivity SLCO1B1, 1 Variant 2008426

Related test

Creatine Kinase, Total, Serum or Plasma 0020010
- Nonspecific indicator of muscle inflammation or damage
- Routine monitoring of creatine kinase level may be considered for individuals who are at risk for myopathy

Disease Overview

Prevalence
- 1-5% of individuals exposed to simvastatin may experience a dose-dependent myopathy (skeletal muscle toxicity)
- Allele frequency varies by ethnicity
  - Middle Eastern – 5%
  - Caucasian – 1-3%
  - Asian – 0-2%
  - African American – 0-2%
  - Other populations – <1%

Symptoms
- May include
  - Myalgia
  - Cramps
  - Myopathy
  - Rhabdomyolysis
- Severe reactions may progress to severe muscle damage with secondary kidney injury

Treatment issues
- Simvastatin is a commonly prescribed hypolipidemic drug used for cholesterol reduction and control
- Testing for statin sensitivity may be helpful for therapy decisions based on risk for muscle toxicity

Physiology

SLCO1B1 c.521T>C variant decreases the transport of simvastatin from the bloodstream into the liver
- Contributes to accumulation of the active drug in the bloodstream

Diagnostic criteria
- Refer to the Electronic Prescription for Simvastatin algorithm (www.ncbi.nlm.nih.gov/pmc/articles/PMC3384438/figure/f1-clpt201257a/. Copyrighted by PharmGKB. Permission has been granted by PharmGKB and Stanford University)

Genetics

Gene – *SLCO1B1*

Inheritance – autosomal co-dominant

Variant – *SLC01B1**5 (c.521T>C) is strongly associated with simvastatin hypersensitivity reaction

Test Interpretation

Sensitivity/specificity
- Clinical sensitivity – drug dependent
- Analytical sensitivity/specificity – >99% for identification of the presence of one or two copies of *SLCO1B1**5

Results
- Positive
  - One or two copies of *SLCO1B1**5 allele detected
    - Increased risk of muscle toxicity
    - Use lowest effective dose or consider an alternative statin
- Negative – *SLCO1B1**5 allele not detected
  - Not predicted to be at increased risk for muscle toxicity

Limitations
- Only the targeted *SLCO1B1* variant will be analyzed
- Diagnostic errors can occur due to rare sequence variations
- Risk of therapeutic failure or adverse reactions with statins may be affected by genetic and nongenetic factors that are not detected by this test
- Genetic testing does not replace the need for therapeutic or clinical monitoring

Reference

Wilke RA, Ramsey LB, et al. The clinical pharmacogenomics implementation consortium: CPIC guideline for SLCO1B1 and simvastatin-induced myopathy. Clin Pharmacol Ther. 2012;92(1):112-117