Protocol

Genetic Testing for Lipoprotein(a) Variant(s) as a Decision Aid for Aspirin Treatment

(20470)

Medical Benefit		**Effective Date**: 10/01/11	**Next Review Date**: 07/21
Preauthorization	No	**Review Dates**: 07/11, 07/12, 07/13, 07/14, 07/15, 07/16, 07/17, 07/18, 07/19, 07/20	

This protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With a high risk of thrombosis	Interventions of interest are: • Genetic testing for the LPA rs3798220 variant	Comparators of interest are: • Standard clinical management without genetic testing	Relevant outcomes include: • Test validity • Medication use • Morbid events

DESCRIPTION

Lipoprotein(a) (LPA) is a lipid-rich particle similar to low-density lipoprotein and has been determined to be an independent risk factor for coronary artery disease. Patients with a positive test for the LPA genetic variant, rs3798220, have a higher risk for thrombosis and therefore may derive greater benefit from the antithrombotic properties of aspirin. As a result, testing for the rs3798220 variant has been proposed as a method of stratifying benefit from aspirin treatment.

SUMMARY OF EVIDENCE

For individuals who have a high risk of thrombosis who receive genetic testing for LPA rs3798220 variant, the evidence includes observational studies. Relevant outcomes are test validity, medication use, and morbid events. The LPA minor allele, rs3798220, is associated with higher levels of LPA and a higher risk for cardiovascular events. This allele is infrequent in the population and is associated with a modest increase in cardiovascular risk in the general population. Testing for this allele is commercially available, but performance characteristics are uncertain, and standardization of testing has not been demonstrated. Several observational studies have reported that this variant is an independent risk factor for cardiovascular disease, but some studies have not reported a significant association. Evidence from a post hoc analysis of the Women's Health Study reported that carriers of the allele might derive greater benefit from aspirin therapy compared with non-carriers. It is unclear whether this information, which derives from genetic testing, leads to changes in management; in particular, it cannot be determined from available evidence whether deviating from current guidelines on aspirin therapy based on LPA genetic testing improves outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

The use of genetic testing for the LPA rs3798220 allele (LPA-Aspirin Genotype) is considered **investigational** in patients who are being considered for treatment with aspirin to reduce risk of cardiovascular events.

BACKGROUND

LIPOPROTEIN(a)

Extensive epidemiologic evidence has determined that lipoprotein(a) (LPA) blood level is an independent risk factor for cardiovascular disease. The overall risk associated with LPA appears to be modest, and the degree of risk may be mediated by other factors such as low-density lipoprotein levels and/or hormonal status.

Over time, a person's LPA levels remain relatively stable; however, levels have been known to vary up to 1,000-fold between different people, and this is most likely due to genetics. A single nucleotide variant in the LPA gene, LPA rs3798220, has been associated with both elevated LPA levels and an increased risk of cardiovascular disease. This variant substitutes methionine for isoleucine at amino acid position 4399 and is also called I4399M. Mendelian randomization studies have supported the hypothesis that this genetic variant, and the subsequent increase in LPA levels, are causative of cardiovascular disease.

Aspirin is a well-established treatment for patients with known coronary artery disease. It also is prescribed as primary prevention for some patients who are at increased risk of coronary artery disease. Current recommendations for primary prevention consider the future risk of cardiovascular events weighed against the bleeding risk of aspirin. The U.S. Preventive Services Task Force 2013 final guidelines recommended aspirin for men "age of 45 to 79 years when the potential benefit due to reduction in myocardial infarctions outweighs the potential harm due to an increase in gastrointestinal hemorrhage"; the Task Force made the same recommendation for women between the ages of 55 and 79 years.[1] Given such guidelines that recommend individualizing the risk-benefit ratio of aspirin therapy, additional tools that could aid in better defining the benefits of aspirin, and/or the risk of bleeding, have potential utility for clinicians who are making decisions about aspirin therapy.

The Cardio IQ® LPA Aspirin Genotype test is a commercially available genetic test (Berkeley HeartLab, a Quest Diagnostics service) that detects the presence of the rs3798220 allele. Patients with a positive test for rs3798220 have a higher risk for thrombosis and therefore may derive more benefit from the antithrombotic properties of aspirin. It has been proposed that the additional information obtained from the test may aid physicians in better estimating the benefit and risk of aspirin therapy and therefore may aid in deciding whether to prescribe aspirin for individual patients.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Berkeley HeartLab/Quest Diagnostics is certified under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

Services that are the subject of a clinical trial do not meet our Technology Assessment and Medically Necessary

Services Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment and Medically Necessary Services Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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