Protocol

DNA-Based Testing for Adolescent Idiopathic Scoliosis

(20474)

Medical Benefit		**Effective Date**: 04/01/12	**Next Review Date**: 09/17
Preauthorization	No	**Review Dates**: 01/12, 09/12, 09/13, 09/14, 09/15, 09/16	

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
Patients/individuals with: • Adolescent idiopathic scoliosis	Interventions of interest are: • Clinical management with prognostic testing with an algorithm incorporating SNP-based testing	Comparators of interest are: • Routine clinical management	Relevant outcomes include: • Change in disease severity • Morbid events • Symptoms

SNP: single nucleotide polymorphism.

Description

Adolescent idiopathic scoliosis (AIS) is a disease of unknown etiology that causes mild-to-severe spinal deformity in approximately 1% to 3% of adolescents. While there is controversy about the value of both screening and treatment, patients once diagnosed are frequently closely followed. In cases with significant progression of curvature, both medical (bracing) and surgical (spinal fusion) interventions are considered. Classification tables for likelihood of progressive disease have been constructed to assist in managing patients, but these have not proven to be highly reliable and the impact of their use on outcomes is unknown. The ScoliScore™ AIS prognostic DNA-based test (Transgenomic, Omaha, NE) that uses an algorithm incorporating results of testing for 53 single-nucleotide polymorphisms (SNPs), along with the patient's presenting spinal curve (Cobb angle), to generate a risk score (range, 1-200), which can be used qualitatively or quantitatively to predict the likelihood of spinal curve progression.

Summary of Evidence

For use of (single-nucleotide polymorphisms) SNP based testing in the management of patients with existing AIS, the evidence consists of a number of cross-sectional studies reporting on the clinical validity of the ScoliScore test, along with cross-sectional studies reporting on the association with SNPs in various genes and scoliosis progression. Preliminary clinical validity results for the ScoliScore™ AIS prognostic DNA-based test indicate a high negative predictive value and an uncertain positive predictive value. A single study has been published reporting a high negative predictive value for ruling out the possibility of progression to severe curvature in a population with a low baseline likelihood of progression. It is not clear if the increase in predictive accuracy provided by testing is statistically or clinically meaningful. Other genetic studies have not demonstrated

significant associations between the SNPs used in the ScoliScore and scoliosis progression. Studies have identified additional SNPs that may be associated with AIS severity, but these associations have not been reliably replicated. The clinical validity of DNA-based testing (either through testing of individual SNPs or through an algorithm incorporating SNP results) for predicting scoliosis progression disorder in patients with AIS condition has not been established because studies of the association of DNA-based testing and scoliosis progression have had mixed findings.

There is no direct evidence demonstrating that use of this test results in changes in management that improve outcomes. The value of early identification and intervention(s) for people at risk for progression of disease is unclear. Therefore, the evidence is insufficient to permit conclusions about the clinical utility of DNA-based predictive testing for scoliosis.

Policy

DNA-based prognostic testing for adolescent idiopathic scoliosis is considered **investigational**.

Background

AIS is the most common pediatric spinal deformity, affecting 1% to 3% of adolescents.[1] This disease, of unknown etiology, occurs in otherwise healthy children with the onset of, and highly correlated with, the adolescent growth spurt. The vertebrae become misaligned such that the spine deviates from the midline laterally and becomes rotated axially. Deviation can occur anteriorly (a lordotic deviation), posteriorly (a kyphotic deviation), or laterally. Although AIS affects females and males in a nearly 1:1 ratio, progression to severe deformity occurs more often in females. Because the disease can have rapid onset and produce considerable morbidity, school screenings have been recommended. However, screening remains somewhat controversial, with conflicting guidelines supporting this practice or alternatively suggesting an insufficiency of evidence for this.

Diagnosis is established by radiologic observation in adolescents (age 10 years until the age of skeletal maturity) of a lateral spine curvature of 10° or more, as measured using the Cobb angle.[2] The Cobb angle is defined as the angulation measured between the maximally tilted proximal and distal vertebrae of the curve. Curvature is considered mild (< 25°), moderate (25°-40°), or severe (> 40°) in a patient still growing. Once diagnosed, patients must be monitored over several years, usually with serial radiographs for curve progression. If the curve progresses, spinal bracing is the generally accepted first-line treatment. If the curve progresses in spite of bracing, spinal fusion may be recommended.

Curve progression has been linked to a number of factors, including sex, curve magnitude, patient age, and skeletal maturity. Risk tables have been published by Lonstein and Carlson[3] and Peterson and Nachemson[4] to help in triage and treatment decision making about patients with AIS. Tan et al[5] recently compared a broad array of factors and concluded that using 30° as an end point, initial Cobb angle magnitude produces the best prediction of progression outcome.

The familial nature of this disease was noted as early as 1968.[6] About one-quarter of patients report a positive family history of disease, and twin studies have consistently supported shared genetic factors.[1] Genome-wide linkage studies have reported multiple chromosomal regions of interest, often not replicated. Ogilvie has recently suggested AIS is a complex polygenic trait.[7] Ogilvie et al at Axial Diagnostics published a study evaluating an algorithm using 53 SNP markers identified from unpublished genome-wide association studies to identify patients unlikely to exhibit severe progression in curvature versus those at considerable risk for severe progression. The clinical validity of this assay has recently been reported in a retrospective case control cohort study using this algorithm.[2]

The ScoliScore™ AIS prognostic DNA-based test (Transgenomic, Omaha, NE), which uses an algorithm incorporating results of testing for 53 SNPs, along with the patient's presenting spinal curve (Cobb angle), to generate a risk score (range, one to 200), can be used qualitatively or quantitatively to predict the likelihood of spinal curve progression. The test is intended for white (Caucasian) patients, aged nine to 13 years, with a primary diagnosis of AIS with a mild scoliotic curve (defined as < 25°).

Regulatory Status

The ScoliScore™ AIS prognostic DNA-based test (originally developed by Axial Biotech, Salt Lake City, UT; test rights acquired by Transgenomic in 2013) has not been approved or cleared by the U.S. Food and Drug Administration but is being offered as a laboratory-developed test. The laboratory performing this test is accredited by the Centers for Medicare and Medicaid under the Clinical Laboratory Improvement Amendments of 1988.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment 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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