DNA-Based Testing for Adolescent Idiopathic Scoliosis

**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 screening and treatment, once diagnosed, patients are frequently closely followed. In cases with significant progression of curvature, both medical (bracing) and surgical (spinal fusion) interventions are considered. The ScoliScore AIS prognostic DNA-based test uses an algorithm incorporating results of testing for 53 single nucleotide variants (SNVs), 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.

**OBJECTIVE**
The objective of this review is to evaluate whether specific DNA-based algorithms and other genetic tests are prognostic in the management of adolescent idiopathic scoliosis.

**POLICY STATEMENT**
DNA-based prognostic testing for adolescent idiopathic scoliosis is considered investigative.

**POLICY GUIDELINES**

**GENETIC COUNSELING**
Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual’s family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

**BENEFIT APPLICATION**
Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.
Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient’s existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

The ScoliScore™ AIS Prognostic Test was originally developed by Axial Biotech with test rights acquired by Transgenomic in 2013. In 2015, Transgenomic divested its Genetic Assays & Platforms Business Unit to ADSTEC Corp.8 In June 2017, Transgenomic was acquired by Precipio Diagnostics in a reverse merger transaction.8 It does appear that the test remains commercially available.

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. 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.

RATIONALE

Summary of Evidence

For individuals with AIS who receive clinical management with prognostic testing using an algorithm incorporating SNV-based testing, the evidence includes cross-sectional studies reporting on the clinical validity of the ScoliScore test, along with cross-sectional studies reporting on the association between SNVs in various genes and scoliosis progression. The relevant outcomes are symptoms, morbid events, and change in disease status. A single study on the clinical validity for the ScoliScore AIS prognostic DNA-based test has reported 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 SNVs used in the ScoliScore and scoliosis progression. Studies have identified additional SNVs 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 SNVs or an algorithm incorporating SNV results) for predicting scoliosis progression in patients with AIS has not been established. 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 the disease and whether laboratory testing improves disease identification beyond clinical evaluation are unknown. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

The Scientific Society on Scoliosis Orthopaedic and Rehabilitation Treatment (2011) issued guidelines on the conservative treatment of idiopathic scoliosis.22 These guidelines did not address the role of DNA-based prognostic testing. A 2016 guideline update mentions a single prognostic genetic test (ScoliScore) and states that, while initial results have been promising, the generalizability is considered uncertain.
FEP 2.04.74 DNA-Based Testing for Adolescent Idiopathic Scoliosis

U.S. Preventive Services Task Force Recommendations
The U.S. Preventive Services Task Force (2004) recommended against the routine screening of asymptomatic adolescents for idiopathic scoliosis (grade D recommendation). This recommendation is currently being updated. No Task Force recommendations for DNA-based testing for adolescent idiopathic scoliosis were identified.

Medicare National Coverage
There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.

POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2012</td>
<td>New Policy</td>
<td>Updated with literature review, references updated no change in policy statement.</td>
</tr>
<tr>
<td>December 2013</td>
<td>Update Policy</td>
<td>Policy updated with literature review through June 6, 2014; references 11-15 added. No change to policy statement.</td>
</tr>
</tbody>
</table>

The policies in this document are subject to change. Please refer to the FEP Medical Policy Manual for the most current information.