FEP 2.04.74 DNA-Based Testing for Adolescent Idiopathic Scoliosis

Effective Date: April 15, 2018

Related Policies:
2.01.83 Interventions for Progressive Scoliosis

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.

FDA REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Exome or genome sequencing tests as a clinical service are available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

POLICY STATEMENT

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

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.

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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).

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. 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

In 2011, the Scientific Society on Scoliosis Orthopaedic and Rehabilitation Treatment issued guidelines on the conservative treatment of idiopathic scoliosis.[22] These guidelines did not address the role of DNA-based prognostic testing.

U.S. Preventive Services Task Force Recommendations

In 2004, the U.S. Preventive Services Task Force recommended against the routine screening of asymptomatic adolescents for idiopathic scoliosis (grade D recommendation).[23] 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

1. Weinstein SL, Dolan LA, Cheng JC, et al. Adolescent idiopathic scoliosis. *Lancet.* May 3 2008;371(9623):1527-1537. PMID 18456103
2. Ward K, Ogilvie JW, Singleton MV, et al. Validation of DNA-based prognostic testing to predict spinal curve progression in adolescent idiopathic scoliosis. *Spine (Phila Pa 1976).* Dec 1 2010;35(25):E1455-1464. PMID 21102273
3. Lonstein JE, Carlson JM. The prediction of curve progression in untreated idiopathic scoliosis during growth. *J Bone Joint Surg Am.* Sep 1984;66(7):1061-1071. PMID 6480635
4. Peterson LE, Nachemson AL. Prediction of progression of the curve in girls who have adolescent idiopathic scoliosis of moderate severity. Logistic regression analysis based on data from The Brace Study of the Scoliosis Research Society. *J Bone Joint Surg Am.* Jun 1995;77(6):823-827. PMID 7782354
5. Tan KJ, Moe MM, Vaithinathan R, et al. Curve progression in idiopathic scoliosis: follow-up study to skeletal maturity. *Spine (Phila Pa 1976).* Apr 1 2009;34(7):697-700. PMID 19333102
6. Wynne-Davies R. Familial (idiopathic) scoliosis. A family survey. *J Bone Joint Surg Br.* Feb 1968;50(1):24-30. PMID 5641594
7. Ogilvie J. Adolescent idiopathic scoliosis and genetic testing. *Curr Opin Pediatr.* Feb 2010;22(1):67-70. PMID 19949338
8. BLL Partners LLC. Transgenomic Finalizes Divestment of its Genetic Assays & Platforms Business Unit. 2015; https://www.sec.gov/Archives/edgar/data/1043961/000114420415068699/v425907_ex99-1.htm. Accessed December 15, 2017.
9. Bloomberg. Life Sciences Tools and Services: Company Overview of Transgenomic, Inc. 2017; https://www.bloomberg.com/research/stocks/private/snapshot.asp?privcapId=416660. Accessed December 15, 2017.
10. Roye BD, Wright ML, Matsumoto H, et al. An independent evaluation of the validity of a DNA-based prognostic test for adolescent idiopathic scoliosis. *J Bone Joint Surg Am.* Dec 16 2015;97(24):1994-1998. PMID 26677232
11. Roye BD, Wright ML, Williams BA, et al. Does ScoliScore provide more information than traditional clinical estimates of curve progression? *Spine (Phila Pa 1976).* Dec 1 2012;37(25):2099-2103. PMID 22614798
12. Bohl DD, Telles CJ, Ruiz FK, et al. A genetic test predicts providence brace success for adolescent idiopathic scoliosis when failure is defined as progression to >45 degrees. *Clin Spine Surg.* Apr 2016;29(3):E146-150. PMID 27007790
13. Tang QL, Julien C, Eveleigh R, et al. A replication study for association of 53 single nucleotide polymorphisms in ScoliScore test with adolescent idiopathic scoliosis in French-Canadian population. *Spine (Phila Pa 1976).* Apr 15 2015;40(8):537-543. PMID 25646748
14. Xu L, Huang S, Qin X, et al. Investigation of the 53 markers in a DNA-based prognostic test revealing new predisposition genes for adolescent idiopathic scoliosis. *Spine (Phila Pa 1976).* Jul 15 2015;40(14):1086-1091. PMID 25811265
15. Xu L, Qin X, Sun W, et al. Replication of association between 53 single-nucleotide polymorphisms in a DNA-based diagnostic test and AIS progression in Chinese Han population. *Spine (Phila Pa 1976).* Feb 2016;41(4):306-310. PMID 26579958
16. Ogura Y, Takahashi Y, Kou I, et al. A replication study for association of 53 single nucleotide polymorphisms in a scoliosis prognostic test with progression of adolescent idiopathic scoliosis in Japanese. *Spine (Phila Pa 1976).* Jul 15 2013;38(16):1375-1379. PMID 23591653
17. Noshchenko A, Hoffecker L, Lindley EM, et al. Predictors of spine deformity progression in adolescent idiopathic scoliosis: A systematic review with meta-analysis. *World J Orthop.* Aug 18 2015;6(7):537-558. PMID 26301183
18. Sharma S, Gao X, Londono D, et al. Genome-wide association studies of adolescent idiopathic scoliosis suggest candidate susceptibility genes. *Hum Mol Genet.* Apr 1 2011;20(7):1456-1466. PMID 21216876
19. Fendri K, Patten SA, Kaufman GN, et al. Microarray expression profiling identifies genes with altered expression in adolescent idiopathic scoliosis. *Eur Spine J.* Jun 2013;22(6):1300-1311. PMID 23467837
20. Jiang J, Qian B, Mao S, et al. A promoter polymorphism of tissue inhibitor of metalloproteinase-2 gene is associated with severity of thoracic adolescent idiopathic scoliosis. *Spine (Phila Pa 1976).* Jan 1 2012;37(1):41-47. PMID 21228746
21. Qiu Y, Mao SH, Qian BP, et al. A promoter polymorphism of neurotrophin 3 gene is associated with curve severity and bracing effectiveness in adolescent idiopathic scoliosis. *Spine (Phila Pa 1976).* Jan 15 2012;37(2):127-133. PMID 22158057

22. Negrini S, Aulisa AG, Aulisa L, et al. 2011 SOSORT guidelines: orthopaedic and rehabilitation treatment of idiopathic scoliosis during growth. *Scoliosis.* Jan 20 2012;7(1):3. PMID 22264320
23. U.S. Preventive Services Task Force (USPSTF). Idiopathic Scoliosis in Adolescents: Screening. 2004; https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/idiopathic-scoliosis-in-adolescents-screening. Accessed December 1, 2017.

POLICY HISTORY

Date	Action	Description
March 2012	New Policy	
December 2012	Update Policy	Updated with literature review, references updated no change in policy statement.
December 2013	Update Policy	Policy updated with literature review; reference 9 added. Policy statement unchanged.
September 2014	Update Policy	Policy updated with literature review through June 6, 2014; references 11-15 added. No change to policy statement
September 2015	Update Policy	Policy updated with literature review; reference 11 added. Policy statement unchanged.
March 2017	Update Policy	Policy updated with literature review through November 7, 2016; references 9, 11, and 13-14 added. Policy statement unchanged.
March 2018	Update Policy	Policy updated with literature review through November 21, 2017; references 8-9 added; note 22 updated. Policy statement unchanged.