2.04.74	DNA-Based Testing for Adolescent Idiopathic Scoliosis		
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Section:	2.0 Medicine	**Page:**	Page 1 of 12

Policy Statement

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

Policy Guidelines

Genetic Counseling
Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Coding
The ScoliScore™ AIS (adolescent idiopathic scoliosis) prognostic DNA-based test has a specific CPT code:
- **0004M**: Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score

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.

Related Policies

- Interventions for Progressive Scoliosis

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

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. 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

Background
Adolescent Idiopathic Scoliosis
Adolescent idiopathic scoliosis (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 rotates axially. The 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 a rapid onset and produce considerable morbidity, school screenings have been recommended. However, screening remains somewhat controversial, with conflicting guidelines supporting and not supporting this practice.

Diagnosis
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 angle measured between the maximally tilted proximal and distal vertebrae of the curve. The 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.

Treatment
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, by Lonstein and Carlson (1984)[3] and Peterson and Nachemson (1995),[4] help in triage and treatment decision making about patients with AIS. Tan et al (2009) 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.[5]

Genetic Associations and Scoliosis
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 (2010) has suggested AIS is a complex polygenic trait.[7] Ogilvie et al at Axial Diagnostics published a study evaluating an algorithm using 53 single nucleotide variant (SNV) markers identified from unpublished genome-wide association studies to differentiate patients unlikely to exhibit severe progression in curvature from those at considerable risk for severe progression. The clinical validity of this assay was reported in a 2010 retrospective case-control cohort study using this algorithm.[2]

ScoliScore AIS
The ScoliScore AIS prognostic DNA-based test (Transgenomic), which uses an algorithm incorporating results of testing for 53 SNVs, along with the patient's presenting spinal curve

(Cobb angle), to generate a risk score (range, 1-200), can be used qualitatively or quantitatively to predict the likelihood of spinal curve progression. The test is intended for white (Caucasian) patients, ages 9 to 13 years, with a primary diagnosis of AIS with a mild scoliotic curve (defined as <25°).

The development and validation of the ScoliScore SNV-based prognostic algorithm were described in 2010 by Ward et al in the industry-sponsored study discussed above.[2] The prognostic algorithm was developed in a cohort of 2192 female patients from prior studies. Candidate genes were selected based on previous genome-wide association studies data from the same investigators. The independent effect of each SNV and clinical factors (initial Cobb angle) and all gene-gene interaction terms were tested in a stepwise logistic regression using a backward-selection procedure and then using a forward-selection procedure. The final predictive model included 53 SNV markers, multiple gene-gene interaction terms, and the patient's initial Cobb angle. Prediction probabilities were converted to a numeric score ranging from 1 to 200. A priori, low-risk of progression was determined to be less than 1%; from the generation cohort, a score of less than 41 was selected as an initial cutoff.

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.[9] It does appear that the test remains commercially available.

Literature Review
See Appendix Table 1 for genetic testing categories.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Prognostic Testing For Adolescent Idiopathic Scoliosis
Clinical Context and Test Purpose
The purpose of the ScoliScore AIS prognostic DNA-based test and other individual single nucleotide variant (SNV)–based tests for scoliosis prognosis is primarily to determine whether patients with scoliosis are at higher likelihood for curve progression. Such patients could undergo more frequent surveillance than they would without testing. The current standard for management of patients with scoliosis that is not severe enough to undergo bracing or surgery is observation with routine radiographic or clinical follow-up.

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is individuals with a diagnosis of adolescent idiopathic scoliosis (AIS) that is not yet severe enough to require bracing or surgery.

Interventions
The intervention of interest is testing for SNVs, including testing with the specific ScoliScore AIS prognostic test, which uses multiple SNVs along with the Cobb angle in an algorithm.

Comparators
The following practices are currently being used to make decisions about follow-up for patients with AIS that is not severe enough to require bracing or surgery: routine radiographic or clinical follow-up, at an interval that is generally determined by the individual patient and physician in shared decision making. The test is an adjunct to existing clinical information and test results.

Outcomes
The general outcomes of interest are change in disease severity (ie, progression in scoliosis curve), morbid events (ie, development of severe scoliosis, which is generally considered to be a Cobb angle >40°), or back pain.

Beneficial outcomes resulting from a true test result, if a true test result is followed by earlier detection of scoliosis by either clinical or radiologic testing, would be earlier detection and treatment of scoliosis. Potential harms from the test include those from a false-positive or a false-negative: false-positive results could lead to increased clinical or radiologic surveillance, while false-negative tests could lead to premature stopping of surveillance.

Timing
The relevant follow-up period depends on the timing of presentation relative to the cessation of growth; however, it is generally over the course of 2 to 3 years.

Setting
Patients would be seen in the outpatient setting.

Simplifying Test Terms
There are 3 core characteristics for assessing a medical test. Whether imaging, laboratory, or other, all medical tests must be:
- Technically reliable
- Clinically valid
- Clinically useful.

Because different specialties may use different terms for the same concept, we are highlighting the core characteristics. The core characteristics also apply to different uses of tests, such as diagnosis, prognosis, and monitoring treatment.

Diagnostic tests detect presence or absence of a condition. Surveillance and treatment monitoring are essentially diagnostic tests over a time frame. Surveillance to see whether a condition develops or progresses is a type of detection. Treatment monitoring is also a type of detection because the purpose is to see if treatment is associated with the disappearance, regression, or progression of the condition.

Prognostic tests predict the risk of developing a condition in the future. Tests to predict response to therapy are also prognostic. Response to therapy is a type of condition and can be either a beneficial response or adverse response. The term predictive test is often used to refer to response to therapy. To simplify terms, we use prognostic to refer both to predicting a future condition or predicting a response to therapy.

Technically Reliable
Assessment of technical reliability focuses on specific tests and operators and requires review of unpublished and often proprietary information. Review of specific tests, operators, and unpublished data are outside the scope of this evidence review and alternative sources exist. This evidence review focuses on the clinical validity and clinical utility.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Study Selection Criteria
For the evaluation of the clinical validity of the ScoliScore AIS test and other SNV-related tests for scoliosis progression, studies that meet the following eligibility criteria were considered:
- Reported on the accuracy of the marketed version of the ScoliScore test or describes the specific SNVs measured;
- Patient or sample clinical characteristics were described;
- Patient or sample selection criteria were described.

Clinical Validity of ScoliScore SNV-Based Testing
The development of the ScoliScore algorithm is discussed briefly in the Background section (Ward et al, 2010).[2]

In 2010, Ward et al described the validation of the ScoliScore algorithm in a group of patients who had a diagnosis of AIS but who had not been previously involved in any AIS or genotype-related studies.[2] These subjects were preselected by curvature severity (mild, moderate, severe) and assigned into 3 cohorts identified as: (1) a screening cohort of white females; (2) a spinal surgery practice cohort of white females; and (3) a male cohort. Inclusion and exclusion criteria were cited as being used, but not explicitly provided, although a component of cohort development was matching of disease prevalence by severity according to that expected from a review of the literature or survey of clinical practices. Ward provided minimal information about the demographics of patients assigned to each cohort. Assignment of curvature severity was performed using the expert opinion of a single orthopedic spine surgeon and was supplemented by an external blinded review of the spinal surgery practice patients using an outside panel of 3 independent scoliosis experts.

The screening cohort was composed of 277 patients recruited to ensure 85% exhibited mild or improved curves, 12% moderate curve progression, and 3% severe curve progression. Using a risk score cutoff of 41 or less, the predictive value of a negative test (defined as identification of patients without severe curve progression) was 100% (95% confidence interval [CI], 98.6% to 100%). No analysis was performed to demonstrate whether this was a statistically significant improvement in prediction of negatives, given the low initial prevalence of patients expected to exhibit severe progression.

The spine surgery practice cohort was composed of 257 patients recruited to ensure 68% exhibited mild or improved curves, 21%, moderate curve progression, and 11% severe curve progression. Using the risk score cutoff of 41 or less, the predictive value of a negative test (defined as identification of patients without severe curve progression) was 99% (95% CI, 95.4% to 99.6%). No analysis was performed to demonstrate whether this was a statistically significant improvement in prediction of negatives. In the male cohort (n=163), the prevalence of patients with progression to severe curvature was 11% before testing. The negative predictive value after testing was 97% (95% CI, 93.3% to 99%).

Although there are a description of positive predictive value calculations using a risk score cutoff of 190 or more, recruitment of patients into this category appears to have been derived from patients pooled from different and undescribed sources, making interpretation difficult.

In 2015, Roye et al reported on an independent validation of the ScoliScore algorithm in a sample of 126 patients with AIS who were enrolled at 2 centers using a retrospective cohort design.[10] Eligible patients had AIS with an initial Cobb angle of 10° to 25° and were white with skeletal immaturity. ScoliScore results were provided as continuous and categorical variables; categories were low (1-50 points), intermediate (51-179 points), or high (180-200 points) risk for progression. Outcomes were defined as progression (curve progression to >40° or requirement for spinal fusion) or nonprogression (reached skeletal maturity without curve progression >40°). The mean ScoliScore overall was 103. In unadjusted analysis, the continuous ScoliScore value was not significantly associated with curve progression (odds ratio [OR], 0.999; 95% CI, 0.991 to

1.006; p=0.664). The proportion of patients with curve progression did not differ significantly by ScoliScore risk group. The ScoliScore test positive predictive value and negative predictive value were 27% (95% CI, 9% to 55%) and 87% (95% CI, 69% to 96%), respectively.

In 2012, Roye et al reported retrospective results for 91 patients evaluated using ScoliScore.[11] Although they noted a positive correlation between Cobb angle and ScoliScore results (r=0.581, p<0.001), ScoliScore appeared to be providing information very different from that observed using a standard risk score, with a marked increase in low-risk patients and a decrease in high-risk patients. However, no clinical end points were examined in association with classification results, and so interpretation of results observed remains unclear.

In 2016, Bohl et al reported on results of a small retrospective cohort study comparing ScoliScore results among patients with AIS undergoing bracing for scoliosis that had progressed to those undergoing bracing without progression.[12] Authors contacted 25 patients with AIS treated at a single institution who underwent nighttime bracing; 16 subjects provided saliva samples to allow ScoliScore testing. Authors reported that the 8 patients whose curves progressed to greater than 45° had a higher mean ScoliScore than those whose curves did not progress (176 vs 112, respectively; p=0.03). No patient with a ScoliScore below 135 progressed to greater than 45°. The interpretation of these results is unclear due to the study's small size and potential for selective response bias.

Studies Assessing SNV Subsets Based on ScoliScore
Some studies have evaluated subsets of the SNVs used in the ScoliScore algorithm. Tang et al (2015)[13] evaluated the association between 25 of the 53 SNVs used in the Ward study (previously described), along with 27 additional SNVs in high linkage disequilibrium with the other SNVs, and severe scoliosis in a case-control study involving 476 AIS patients of French-Canadian background. None of the SNVs was significantly associated with scoliosis severity.

The ScoliScore algorithm was developed and validated in a sample of white patients. Other studies have evaluated the association of specific SNVs from the algorithm in nonwhite populations. For example, in 2015, Xu et al reported on the association between the 53 SNVs in the ScoliScore panel with scoliosis in a retrospective case-control study of 990 female Han Chinese patients with AIS and 1188 age-matched healthy controls.[14] At 4 loci, patients with AIS differed from controls: they had a higher frequency of G alleles at rs12618119 (46.5% vs 40.2%, OR=1.29; 95% CI, 1.15 to 1.46; p<0.001) and A alleles at rs9945359 (22.6% vs 18.4%; OR=1.29; 95% CI, 1.12 to 1.50; p<0.001), and a lower frequency of T alleles at rs4661748 (15.6% vs 19.4%; OR=0.77, 95% CI, 0.66 to 0.90; p<0.001) and C alleles at rs4782809 (42.4% vs 47.4%; OR=0.82, 95% CI, 0.72 to 0.92; p<0.001).

In 2016, Xu et al reported on the association between the 53 SNVs in the ScoliScore panel with scoliosis progression in a retrospective case-control study of 670 female Han Chinese patients with AIS.[15] Patients were identified from a set of patients who visited trialists' scoliosis center for a time period that overlapped with that for the patients in the 2015 Xu study, but it was not specified whether the data overlapped. Of the 670 patients, 313 were assigned to the nonprogression group (defined as a Cobb angle <25° at final follow-up), and 357 were assigned to the progression group (defined as a Cobb angle of >40° at final follow-up). The overall follow-up duration was not specified. At 2 loci, allele frequencies differed between groups: the progression group had a significantly higher frequency of allele A at rs9945359 (25.7% vs 19.5%; OR=1.42; 95% CI, 1.09 to 1.88; p=0.01) and a significantly lower frequency of allele A at rs17044552 (11.5% vs 16.4%; OR=0.65; 95% CI, 0.47 to 0.91; p=0.01).

There was no association between the 53 SNVs in the ScoliScore panel and curve progression in an earlier study (2013) of 2117 Japanese patients with AIS.[16]

Clinical Validity of Other SNV Associations with Scoliosis Prognosis
In addition to studies evaluating the clinical validity of the ScoliScore algorithm specifically, other studies have reported results for associations between SNVs and scoliosis progression. For example, in 2015, Noshchenko et al reported on a systematic review and meta-analysis of predictors of progression in AIS, which included studies evaluating the association between ScoliScore and SNVs and curve progression.[17] In total, reviewers included 25 studies, across a range of physiologic measures. Reviewers selected 2 studies that evaluated ScoliScore—Ward et al (2010)[2] and Bohl et al (2016).[12] Pooled results were presented; however, given the differences in interventions in the studies (Bohl et al evaluated response to bracing), the results are more appropriately considered as individual studies, which are described above in the Clinical Validity of ScoliScore SNV-Based Testing section. Studies evaluating 7 additional SNVs in multiple genes, including *CALM1*, *ER1*, *TPH1*, *IGF1*, *NTF3*, *IL17RC*, and *MTNR1B* (N=7 studies) were included. The level of evidence based on GRADE for the studies was considered very low or low. Estimates for the pooled odds for the association between the variant and the outcome ranged from 1.5 to 3.3. Reviewers concluded that "the levels of association were relatively low with small predictive capacity. All these findings have very low level of evidence due to the limitations of the studies' design and that fact that only one study reported each finding."

Sharma et al (2011) reported genome-wide association study results evaluating 327,000 SNVs in 419 families with AIS.[18] They found 3 loci were significantly associated with scoliosis progression, which did not include any of the 53 SNVs included in the Ward study previously described.

In 2013, Fendri et al reported on results from a case-control study 6 AIS patients and 6 non-AIS controls evaluating differential gene expression profiling in AIS.[19] Gene expression profiles from primary osteoblasts derived from spinal vertebrae of AIS patients (n=6) were compared with profiles from the same cells collected from age- and sex-matched previously healthy patients who underwent spinal surgery for trauma (n=6). One hundred forty-five genes displayed significant expression changes in AIS osteoblasts compared with non-AIS osteoblasts. After hierarchical clustering gene ontology analysis, the authors identified 5 groups based on molecular function and biologic process that fell into 4 pathways: developmental/growth differentiation of skeletal elements (ie, *HOXB8*, *HOXB2*, *MEOX2*, *PITX1*), cellular signaling (ie, *HOXA11*, *BARX1*), connecting structural integrity of the extracellular matrix to the structural integrity of a bone or a muscle fiber (ie, *COMP*, *HOXA2*, *HOXA11*), and cellular signaling and cartilage damage (*GDF15*).

Studies have also associated variants in the promoter regions of tissue inhibitor of metalloproteinase-2 and neurotrophin-3 with AIS severity in Chinese populations.[20,21] Replication of these genetic associations is needed.

Section Summary: Clinically Valid
Four retrospective case-control studies have reported on the clinical validity of the marketed ScoliScore test; two of them permitted a determination of the association of the test with curve progression, and they had conflicting results and were limited by their retrospective designs. A number of additional studies have reported on the association between scoliosis progression or presence and various other SNVs, with inconsistent results. The evidence is insufficient to conclude clinical validity.

Clinically Useful
A test is clinically useful if use of the results inform management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing. No studies examining the impact of DNA-based predictive testing for scoliosis on health outcomes were identified. 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. It is not possible to construct a chain of evidence for clinical utility due to the lack of clinical validity.

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
Clinical Input from Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests from Blue Cross Blue Shield Association, input was received from 2 specialty societies and 4 academic medical centers in 2012. All agreed with this policy and indicated that DNA-based prognostic testing for adolescent idiopathic scoliosis (ScoliScore) should be considered investigational.

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. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Unpublished			
NCT01776125	Genetic Evaluation for the Scoliosis Gene(s) in Patients With Neurofibromatosis 1 and Scoliosis	100	Aug 2015 (completed)

NCT: national clinical trial.

Appendix

Appendix Table 1. Categories of Genetic Testing Addressed in 2.04.74

Category	Addressed
1. Testing of an affected individual's germline to benefit the individual	
1a. Diagnostic	
1b. Prognostic	X
1c. Therapeutic	
2. Testing cancer cells from an affected individual to benefit the individual	
2a. Diagnostic	
2b. Prognostic	
2c. Therapeutic	
3. Testing an asymptomatic individual to determine future risk of disease	
4. Testing of an affected individual's germline to benefit family members	
5. Reproductive testing	
5a. Carrier testing: preconception	
5b. Carrier testing: prenatal	
5c. In utero testing: aneuploidy	
5d. In utero testing: familial variants	
5e. In utero testing: other	
5f. Preimplantation testing with in vitro fertilization	

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24. Blue Cross Blue Shield Association. Medical Policy Reference Manual, No. 2.04.74 (January 2018).

Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms

of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

IE
The following services may be considered investigational.

Type	Code	Description
CPT®	0004M	Scoliosis, DNA analysis of 53 single nucleotide polymorphisms (SNPs), using saliva, prognostic algorithm reported as a risk score
HCPCS	None	
ICD-10 Procedure	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action	Reason
08/29/2014	BCBSA Medical Policy adoption	Medical Policy Committee
01/01/2017	Policy revision without position change	Medical Policy Committee
03/01/2017	Policy revision without position change	Medical Policy Committee
03/01/2018	Policy revision without position change	Medical Policy Committee

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.