SENTARA HEALTH PLANS, INC.
CLINICAL CARE SERVICES

Medical Policy: **Medical 34B**

Subject: **Genetic Testing—Pre-Treatment or Post-Intervention**

Also see other Genetic Testing Policies:

See Genetic Testing 34 A	Cancer Prevention, Diagnosis, and Treatment
F5See Genetic Testing 34 C	Cardioneurovascular and Developmental Diagnosis
See Genetic Testing 34 D	Preconceptional /Prenatal /Preimplantation Genetic Testing for Preconceptional /Prenatal /Preimplantation
See Genetic Testing 34 E	Pharmacogenetic Testing
See Genetic Testing 34 F	Medicare Coverage

Effective Date: February 2009

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Covered: **See appropriate benefit document for specific coverage determination.**

Exceptions: **Based on current scientific evidence, the requested test is considered not medically necessary because the result of genetic testing has not been shown to direct clinical management that results in an improvement of clinical outcomes**

- Acute Porphyria: HMBS, CPOX, PPOX genes

- Alport gene testing; (COL4A3 and COL4A4)7/26/16
- Atypical Hemolytic Uremic Syndrome Complement Panel
- Autoimmune lymphoproliferative syndrome ALPS and FAS gene testing ;
- BetaGlobin analysis;
- BIRC4 test is testing for X-linked lymphoproliferative syndrome (XLP), caused by alterations, also known as “mutations," at a specific area within an individual’s genetic information.
- CLCN1 DNA Sequencing Test for Myotonia congenital;
- Charcot Marie Tooth is not medically necessary;
- deCODE T2, is not medically necessary
- deCODE Glaucoma test, is not medically necessary
- Idiopathic Hypercalcemia of Infancy (CYP24A1 gene)
- IFNL3 & INFNL4 Gene Analysis Associated with Hepatitis C Virus Clearance 81400
- Kennedy's disease (KD) or X-linked spinal and bulbar muscular atrophy (SBMA) or spinobulbar muscular atrophy or X-Linked bulbo-spinal atrophy.
- Lactose intolerance (Prometheus Lab LactoType);
- MaculaRisk PGx
- Methylenetetrahydrofolate reductase (NAD(P)H) also known as MTHFR,
- MTHFR (5,10-methylenetetrahydrofolate reductase) (eg, hereditary hypercoagulability) gene analysis, common variants (eg, 677T, 1298C) (**81291**)
- Narcolepsy gene testing DRB1*15, DQA1*0102, and DQB1*0602
- Porphyria cutanea tarda: UROD gene
- Prometheus Crohn’s
- PROMETHEUS Crohn's Prognostic
- Prometheus IBD Serology 7, for Irritable Bowel Disease
- PROMETHEUS IBD sgi Diagnostic
- Prometheus Thiopurine Metabolites
- Proove Narcotic Risk, Drug Metabolism and Pain Perception Profiles
- Repeat/Duplicative genetic testing
- Transforming Growth Factor Beta-Induced (TGFBI)
- Whole Exome Sequencing (**WES**) all indications,
- Exome Sequence Analysis (**81415, 81416, 81417**)
- Whole-genome sequencing in which a member’s entire DNA is sequenced,
- Genome Sequence Analysis (**81425, 81426, 81427**)

Any other test not listed below as covered is considered among those that are not medically necessary.

For BRAF mutation analysis, genotype testing for genetic polymorphisms, orcytochrome P450, see Medical 34 E – Pharmacogenetic Testing.

Authorization: Pre-certification by the plan is required.
Medical Director approval required for Fabry Disease

Definitions:

Autosomal recessive: A genetic condition that appears only in individuals who have received two copies of an autosomal gene, one copy from each parent. The gene is on an autosome, a nonsex chromosome. The parents are carriers who have only one copy of the gene and do not exhibit the trait because the gene is recessive to its normal counterpart gene
X-linked recessive inheritance - hereditary pattern in which a recessive gene on the X chromosome results in the manifestation of characteristics in male offspring and a carrier state in female offspring

Procedure:

Genetic Testing is considered medically necessary for the prevention diagnosis and treatment of patients who meet the following:

- There is an approved mutation specific treatment available;

OR

- There is sufficient Published Scientific Evidence or 3rd party Consensus in the Medical Community that the results of the specific genetic testing improves clinical outcomes.

AND

- After completion of a thorough history, physical examination, pedigree analysis, genetic counseling, relevant diagnostic and biochemical tests (if any), the patient meets criteria for any of the following approved tests: (**criteria are listed individually for each test below)**

A. HPV DNA

OR

B. Factor V Leiden

OR

C. Prothrombin/Factor II Gene Mutation Analysis

OR

D. PCR(polymerase chain reaction) testing for hepatitis C or B;

OR

E. Thiopurine S-Methyltransferase (TPMT)

OR

F. Fabry disease

OR

G. Hemophilia Hemophilia A or B

OR

H. Aplastic anemia (FISH) fluorescence in situ hybridization;

OR

I. HLA-B27 testing.

OR

J. Hereditary Hemachromatosis
.

OR

K. HLA testing to detect genes specific to patients with possible Celiac disease (e.g., Prometheus testing) (No medical review required)

L. Severe Combined Immunodeficiency (SCID) Genetic Testing

M. X-linked lymphoproliferative syndrome (XLP) testing (SHD1A and XIAP Genes)

Criteria of covered tests which were moved to Genetic 34E include: HLA-B 1502; HLA-B 5701; HIV Drug Susceptibility and Resistance Tests; and CYP2C 19 variant of Cytochrome P450.

Clinical Indications:

A. **HPV DNA**
This test is used to detect the human papilloma virus (HPV), which is considered the primary cause of virtually all cervical cancers.

Clinical indications
Covered without criteria.

B. **Factor V Leiden**
Factor V Leiden is a common inherited genetic disorder in which your blood has an increased tendency to form clots (thrombophilia), usually in your veins. Although blood clots can form at any age, for most people the increased risk of clotting doesn't begin until adulthood. Most people with factor V Leiden never develop abnormal clots. However, some people with factor V Leiden develop clots that lead to long-term health problems or are life-threatening. Both men and women can have factor V Leiden, but

women may have an increased tendency to develop blood clots during pregnancy or when taking the hormone estrogen.

Clinical Indications
Covered without criteria.

C. **Prothrombin/Factor II Gene Mutation Analysis**

Clinical Indications:
Covered without criteria.

D. **PCR (Polymerase Chain Reaction) Testing for Hepatitis C or B**

Clinical Indications:
PCR (polymerase chain reaction) testing for hepatitis C or B

Covered without criteria or Pre-authorization.

E. **Thiopurine S-Methyltransferase (TPMT)**
Genotyping and/or Phenotyping as an initial test to predict response to thiopurine drug therapy. (eg. Prometheus TPMT Enzyme, Prometheus TPMT Genetics etc). Activity for Prediction of Response to Thiopurine Drug Therapy for Inflammatory Bowel Disease.

Clinical Indications: Covered without criteria.

F**.** **Fabry Disease**
Fabry disease results from abnormal deposits of a particular fatty substance (called globotriaosylcera-mide) in blood vessel walls throughout the body.

Clinical Indications: Covered for **individual females** on a case by case basis and **requires Medical Director approval.**

G. **Hemophilia A (Factor VIII) or Hemophilia B (Factor IX)**

Clinical Indications:

1. The member displays clinical features, or is at direct risk of inheritance;

AND

2. The result of the test will directly impact the treatment being delivered to the member;

AND

3. After history, physical examination, and completion of conventional diagnostic studies (e.g. Factor VIII, Factor IX levels), a definitive diagnosis remains uncertain.

H**. Aplastic Anemia (FISH) fluorescence in situ hybridization**

Clinical Indications: For work up of possible Aplastic anemia.
Covered without criteria.

I. **HLA-B27** correlating with ankylosing spondylitis and more than 100 disease associations have been made, including many ocular diseases and systemic diseases with specific ocular manifestations. These also include reactive arthritis (previously referred to as Reiter syndrome), inflammatory bowel disease, and psoriatic arthritis.

Clinical Indications:

Covered when used to rule out autoimmune disorders.

J. **Hereditary Hemochromatosis**

Clinical Indications:

Hemochromatosis - HFE gene testing may be indicated when **ALL** of the following are present (1 & 2):

1. Diagnosis or screening of HFE-hereditary hemochromatosis, as indicated by **1 or more** of the following:

   a. Confirmation of diagnosis in adult with clinical suspicion of HFE-related hemochromatosis, as indicated by **1 or more** of the following:

      (1.) Transferrin-iron saturation higher than 45%;
      OR
      (2.) Serum ferritin above upper limit of normal, and other more common causes of elevated ferritin (eg, acute inflammation, alcohol abuse, metabolic syndrome) have been evaluated with inconclusive results,
      OR

(3.) Unexplained chronic liver disease combined with Increased transferrin saturation;

OR

(4.) Porphyria cutanea tarda;

OR

(5.) Chondrocalcinosis;

OR

(6.) Hepatocellular carcinoma;

OR

(7.) Late-onset type 1 diabetes;

OR

b. Screening of siblings or parents of individual homozygous for C282Y mutation;

OR

c. Screening of reproductive partner of individual with HFE-related hemochromatosis;

AND

2. Testing is accompanied by genetic counseling.

K. **HLA haplotype testing to detect genes specific to Celiac disease** are considered medically necessary for patients suspected of having the disease but who have indeterminate serology and/or inconclusive biopsy results (examples include Prometheus HLA-DQA1, HLA-DQB1, HLA-DQ2, HLA-DQ8 testing).

No Medical review required.

L. **Severe Combined Immunodeficiency (SCID) Genetic Testing** for individuals with inconclusive screening results from an immune function test or T cell and B cell counts considered eligible for transplant to confirm diagnosis.

M. **X-linked lymphoproliferative syndrome (XLP) testing (SHD1A and XIAP Genes)** for transplant patients.

N. **HLA-A29 Uveitis - HLA I TYPING ALLELE HR** screening will be paid upon request when ordered to rule out or confirm Birdshot chorioretinopathy (BSCR), a rare form of autoimmune posterior uveitis that affects visual function that if left untreated can lead to sight-threatening complications and loss of central vision.

CPT/HCPCS:**0047U**	Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score
81240	F2 (prothrombin, coagulation factor II) (eg, hereditary hypercoagulability) gene analysis, 20210G>A variant;
81241	F5 (coagulation Factor V) (eg, hereditary hypercoagulability) gene analysis, Leiden variant;
81256	HFE (hemochromatosis) (eg, hereditary hemochromatosis) gene analysis, common variants (eg, C282Y, H63D);
81333	Transforming growth factor beta-induced (TGFBI) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, and R555Q)
81381	HLA Class I typing, high resolution (ie, alleles or allele groups); 1 allele or allele group (eg, B*57:01P), each
81383	HLA Class II typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, HLA-DQB1*06:02P), each
81400	Molecular pathology procedure, Level 1
81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5
81479	Unlisted molecular pathology procedure
85245	Clotting; factor VIII, VW factor, ristocetin cofactor
85246	Clotting; factor VIII, VW factor antigen
85247	Clotting; factor VIII, von Willebrand factor, multimetric analysis
85250	Clotting; factor IX (PTC or Christmas),

REFERENCES

___ Agency for Healthcare Research and Quality (AHRQ)

___ Diagnostic and Therapeutic Technology Assessment (DATTA) Review

_X_ Specialty Association Guidelines

_X_ Government Regulations

_X_ NCD/LCD

___ Specialty Advisors

___ SHC Guidelines

_X_ Literature Review

_X_ Milliman

_X_ Relevant Other Payer Approaches

_X_ Winifred S. Hayes, Inc. __X__ UpToDate

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