SERVICE: Genetic (Genomic) Testing

PRIOR AUTHORIZATION: Required.

POLICY:

Overarching Principles: All genetic testing should be used for predictive, diagnostic or prognostic disease situations. Genetic testing for non-medical purposes, such as paternity, ancestry, genome-wide association studies (GWAS), and non-disease traits, such as baldness, eye color, are NOT medically necessary. Most genetic testing is once per lifetime or once per pregnancy (prenatal testing). When possible, testing should be performed at a contracted/network laboratory. If a non-contracted (out-of-network) laboratory is required, the member should be informed of difference in out-of-pocket charges. In addition, the provider should document the need for an out-of-network laboratory, e.g., targeted testing in another family member, gene not offered at contracted/network laboratory, etc. Finally, medical necessity must be documented for every request.

Requests for genetic/genomic testing will be reviewed using InterQual® whenever possible. If InterQual® does not have an appropriate criterion set for review, the entire request will be processed using this policy in the usual manner.

Coverage for genetic/genomic testing and/or screening may be medically necessary when all of the following criteria are met:

1. Appropriate genetic counseling occurs before and after testing.
   
   Members must have genetic counseling by a practitioner who has expertise in the genetic aspects of the condition being evaluated and who will discuss the results of the test and their clinical implications. Documentation of the counseling will accompany the preauthorization request.

   Evidence of genetic counseling should include, but is not limited to the following:
   
   - discussion of the types of test results (positive, negative, uncertain findings) that could be obtained,
   - identifying problems that are known to occur due to test methodology,
   - evaluation of the members risk for the specific disorder, the differential diagnosis, inheritance patterns, penetrance, variable expressivity and genetic heterogeneity
   - evidence of informed consent
   - a plan for posttest counseling

   Note: genetic counseling must be performed by practitioners NOT employed by testing companies due to conflict of interest.
2. There must be a reasonable expectation, based on family history, pedigree analysis, risk factors, and/or symptomatology, that a genetically inherited or acquired condition exists and the member displays clinical features, or is at direct risk of inheriting the mutation in question (pre-symptomatic) or comes from the appropriate disease-specific population. A three-generation pedigree **MUST** accompany the request for testing, where appropriate, to aid in coverage determination.

3. Knowledge of the presence or absence of the condition would **DIRECTLY** affect medical care of the member:
   a. The disease must be treatable and/or preventable AND
   b. The test results will lead to a change in the intensity of surveillance frequency and/or treatment for that disease.

4. There are often options for single gene testing, multiple gene testing and panel testing.
   a. If a single gene test meets other criteria and will answer the clinical question, SHWP will generally find such a test medically necessary.
   b. If a multigene panel is requested, there must be evidence that there are two or more genes responsible for a specific condition or that there is the possibility that several genes can cause multiple diseases within the family. Most of the genes on the panel should be plausible explanations for the disorder observed.
   c. The smallest plausible gene panel will be authorized, to decrease variants of unknown significance. Broad multi-gene-based panels are not medically necessary when a more focused study is available.
   d. If a panel is chosen, the list of genes should be on the request and in the accompanying documentation to explain why that particular panel was chosen.
   e. Multiple panels tested at the same time are not medically necessary.

5. The test is performed in a CLIA certified laboratory, AND is FDA approved, AND is **recommended by recognized, national guidelines**.

6. The request **MUST** be submitted with the SWHP “Statement of Medical Necessity for Genetic Testing” located at the end of this policy, OR other documentation such as clinical documentation that addresses all of the questions in that document. In particular there must be a clear statement that explains how the test results will improve the medical management of the patient’s condition. The statement “… is medically necessary” does **NOT** meet the criteria since it does not explain the change in management or surveillance that would take place if the test is positive and if it were negative.

**Note**: Genetic/genomic testing for specific germline conditions or mutations is limited to once per lifetime for the specific mutation or panel. Exceptions may be considered if there is a change in guidelines for genes that have not been tested or need reinterpretation of results.

**Tests with specific policy guidance**:

A. **Cell-free DNA screening tests for microdeletions** (CPT 81422) have **NOT** been validated and are not deemed medically necessary.

B. **Whole Genome Sequencing** may be medically necessary to identify or confirm the genetic etiology of a known or unknown disorder in clinically affected neonatal and pediatric patients. Medical necessity will be determined using the generic criteria listed at the beginning of this policy. In most cases whole genome sequencing will not be found medically necessary unless more targeted studies have failed to identify a mutation.

**Genetic Test codes with diagnosis specifications**:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>PA Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>81161</td>
<td>DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed</td>
<td>No PA if Prenatal Dx present</td>
</tr>
<tr>
<td>81220</td>
<td>CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene</td>
<td>No PA if Prenatal Dx present</td>
</tr>
</tbody>
</table>
The following tests considered experimental and investigational and are NOT considered medically necessary:

a. Genetic testing (e.g., presenilin-1 gene, apolipoprotein E epsilon 4 allele, amyloid precursor gene, etc.) for the diagnosis and assessment of persons with Alzheimer disease and related dementias.

b. Genetic testing for complex eye disorders such as age-related macular degeneration and late-onset primary open angle glaucoma, PreDx Diabetes Risk Test™, deCODE T2™, deCODE AF™, deCODE MI™, deCODE Glaucoma, deCODEme Cancer, deCODE BreastCancer™ and BREVAGen™ Breast Cancer Risk Stratification Test deCODE ProstateCancer 9p21MI Check, and deCODEme Cardio.

c. Additional test codes considered experimental and investigational and are NOT considered medically necessary:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Required Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>81230</td>
<td>CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis,</td>
<td>E&amp;I Unproven</td>
</tr>
<tr>
<td>81231</td>
<td>CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis,</td>
<td>E&amp;I Unproven</td>
</tr>
</tbody>
</table>
**GENETIC TESTING**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>E&amp;I Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>81355</td>
<td>VKORC1 (vitamin K epoxide reductase complex, subunit 1) (eg, warfarin metabolism), gene analysis, common variant(s) (eg, -1639G&gt;A, c.173+1000C&gt;T)</td>
<td>Unproven</td>
</tr>
<tr>
<td>81422</td>
<td>Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal, must include analysis of chromosomes 13, 18, and 21</td>
<td>Unproven</td>
</tr>
<tr>
<td>81434</td>
<td>Hereditary retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy), genomic sequence analysis panel, must include sequencing of at least 15 genes, including ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RH0, RP1, RP2, RPE65, RPGR, and USH2A</td>
<td>Unproven</td>
</tr>
<tr>
<td>81440</td>
<td>Nuclear encoded mitochondrial genes (eg, neurologic or myopathic phenotypes), genomic sequence panel, must include analysis of at least 100 genes, including BCS1L, C10orf2, COQ2, COX10, DGUOK, MPV17, OPA1, PDSS2, POLG, POLG2, RRM2B, SCO1, SCO2, SLC25A4, SUCLA2, SUCLG1, TAZ, TK2, and TYMP</td>
<td>Unproven</td>
</tr>
<tr>
<td>81460</td>
<td>Whole mitochondrial genome (eg, Leigh syndrome, mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes [MELAS], myoclonic epilepsy with ragged-red fibers [MERFF], neuropathy, ataxia, and retinitis pigmentosa [NARP], Leber hereditary optic neuropathy [LHON]), genomic sequence, must include sequence analysis of entire mitochondrial genome with heteroplasmy detection</td>
<td>Unproven</td>
</tr>
<tr>
<td>81465</td>
<td>Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed</td>
<td>Unproven</td>
</tr>
<tr>
<td>81470</td>
<td>X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); genomic sequence analysis panel, must include sequencing of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2</td>
<td>Unproven</td>
</tr>
<tr>
<td>81471</td>
<td>X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); duplication/deletion gene analysis, must include analysis of at least 60 genes, including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2</td>
<td>Unproven</td>
</tr>
<tr>
<td>81490</td>
<td>Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity score</td>
<td>Unproven</td>
</tr>
<tr>
<td>81493</td>
<td>Coronary artery disease, mRNA, gene expression profiling by real-time RT-PCR of 23 genes, utilizing whole peripheral blood, algorithm reported as a risk score</td>
<td>Unproven</td>
</tr>
<tr>
<td>81535</td>
<td>Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; first single drug or drug combination</td>
<td>Unproven</td>
</tr>
<tr>
<td>81536</td>
<td>Oncology (gynecologic), live tumor cell culture and chemotherapeutic response by DAPI stain and morphology, predictive algorithm reported as a drug response score; each additional single drug or drug combination (List separately in addition to code for primary procedure)</td>
<td>Unproven</td>
</tr>
<tr>
<td>81539</td>
<td>Oncology (high-grade prostate cancer), biochemical assay of four proteins</td>
<td>Unproven</td>
</tr>
<tr>
<td>81540</td>
<td>Oncology (tumor of unknown origin), mRNA, gene expression profiling by real-time RT-PCR of 92 genes (87 content and 5 housekeeping) to classify tumor into main cancer type and subtype, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a probability of a predicted main cancer type and subtype</td>
<td>Unproven</td>
</tr>
</tbody>
</table>

**Exclusions:**

The following are examples of services that are not covered:

1. Routine, ongoing, or long-term genetic counseling.
2. Genetic testing to determine the paternity of a child.
3. Genetic testing to determine the sex of the child.
4. General population screening for genetic disorders (e.g., cystic fibrosis).

Definitions:
First-degree relative – a blood relative with whom an individual shares approximately 50% of his or her genes, including parents, full siblings and children
Second-degree relative – a blood relative with whom an individual shares approximately 25% of his/her genes, including grandparents, grandchildren, aunts, uncles, nephews, nieces and half-siblings.

MANDATES: None

CODES:  

Important note:
CODES: Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.

<table>
<thead>
<tr>
<th>CPT Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS Codes:</td>
</tr>
<tr>
<td>ICD-10:</td>
</tr>
<tr>
<td>ICD-10 Not covered:</td>
</tr>
</tbody>
</table>

CMS: There is no NCD.

POLICY HISTORY:

<table>
<thead>
<tr>
<th>Status</th>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>08/01/2010</td>
<td>New policy</td>
</tr>
<tr>
<td>Reviewed</td>
<td>12/06/2011</td>
<td>Reviewed.</td>
</tr>
<tr>
<td>Reviewed</td>
<td>12/06/2012</td>
<td>Revised. BRCA added. Criteria revised</td>
</tr>
<tr>
<td>Reviewed</td>
<td>11/14/2013</td>
<td>BRCA criteria updated.</td>
</tr>
<tr>
<td>Reviewed</td>
<td>04/24/2014</td>
<td>Minor updates made.</td>
</tr>
<tr>
<td>Reviewed</td>
<td>07/02/2015</td>
<td>Extensively re-written</td>
</tr>
<tr>
<td>Reviewed</td>
<td>09/08/2016</td>
<td>Clarified criteria; added pharmacogenetics section.</td>
</tr>
<tr>
<td>Update</td>
<td>06/27/2017</td>
<td>Updated criteria for NIPT.</td>
</tr>
<tr>
<td>Reviewed</td>
<td>08/22/2017</td>
<td>Set most testing limit to once per lifetime. Updated criteria. New request form.</td>
</tr>
<tr>
<td>Minor correction</td>
<td>11/28/2017</td>
<td>Removed discussion regarding FIT-DNA stool testing.</td>
</tr>
<tr>
<td>Reviewed</td>
<td>06/26/2018</td>
<td>Significant revision of several coverage topics.</td>
</tr>
<tr>
<td>Addition</td>
<td>02/12/2019</td>
<td>InterQual® to be used instead of policy for five codes.</td>
</tr>
<tr>
<td>Major revision</td>
<td>09/26/2019</td>
<td>Policy re-written to direct reviews to InterQual®</td>
</tr>
</tbody>
</table>

REFERENCES: The following scientific references were utilized in the formulation of this medical policy.

SWHP will continue to review clinical evidence surrounding genetic testing and may modify this policy at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available and they are not included in the list, please forward the reference(s) to SWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

13. ACOG Committee Opinion 690, March 2017: Carrier screening in the age of genomic medicine
15. American College of Obstetricians and Gynecologists Committee Opinion No 691: Carrier screening for genetic conditions carrier screening for genetic conditions 2017
17. American College of Medical Genetics and Genomics Practice Guidelines
SWHP Genetic Testing Prior Authorization Form

Date of Request: ___/___/_______ Date, if procedure has been scheduled: ___/___/_______

Insured Member Information:

Name: ___________________________ SWHP ID #: ___________________ Date of birth: ___/___/_______

Gender: M F

Provider Information:

Requesting Provider Name: ___________________________ Requesting Provider NPI: ___________________________

Requesting Provider Address: _______________________________________________________________________

Office Contact Person: _________________________ Telephone #: ________________ Fax #: ________________

Supplying Provider Information:

Supplying Provider Name: __________________________________________________________________________

Supplying Provider Address: _______________________________________________________________________

Office Contact Person: _________________________ Telephone #: ________________ Fax #: ________________

Genetic Test Information:

Requested Genetic Test:

☐ BRCA 1 and 2, HBOC ☐ Breast expression RNA ☐ Hereditary Hemochromatosis Gene Analysis
☐ Colon Cancer Lynch Syndrome (list genes) ☐ Cystic Fibrosis ☐ Fragile X Syndrome
☐ Huntington’s Disease ☐ Janus Kinase 2(JAK2) ☐ Chromosomal Microarray
☐ Familial Adenomatous Polyposis /Assoc. Polyposis Conditions ☐ Cardiology Gene Expression (AlloMap) ☐ NIPS (non-invasive prenatal screen)
☐ Multigene panel: Please list genes requested

ICD-10 Codes:

CPT Code Test CPT Code Test

<table>
<thead>
<tr>
<th>CPT Code</th>
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</table>
MEDICAL COVERAGE POLICY

SERVICE: Genetic Testing

Policy Number: 037

Effective Date: 12/01/2019
Last Review: 10/17/2019
Next Review Date: 10/17/2020

Medical Information:

Provide information to justify each test requested. (May attach dictation if it contains requested information.)

1) Why is the test appropriate for the patient? _______________________________________________________________
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________

2) Does the beneficiary exhibit clinical features of the mutation in question? If not, has a genetic variant been identified in a
   family member? (May attach dictation if it contains requested information.)
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________

3) Has the patient given informed consent to the genetic test?  □ Yes  □ No

4) Has genetic counseling occurred? □ Yes  □ No  By whom? ______________________________________________________

5) What is the validity of testing and is the testing scientifically sound? (reference or link)
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________

6) Is the patient willing to undergo the increased interventions that may potentially be required because of testing?
   □ Yes  □ No

7) How will the results specifically impact or alter medical management of the patient?
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________
   ____________________________________________________________________________________________________

8) What is the cost of the test? ____________________________________________________________________________

9) Is multigene panel testing more cost efficient than the combined reimbursement for single codes? ________________

Signature of Requesting Provider: ___________________________ Date: ___/___/____