MEDICAL COVERAGE POLICY	
SERVICE: Genetic Testing	
Policy Number:	**037**
Effective Date:	**06/01/2021**
Last Review:	**04/22/2021**
Next Review Date:	**04/22/2022**

Important note:
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

SERVICE: Genetic (Genomic) Testing

PRIOR AUTHORIZATION: Required.

POLICY: Not all Plans cover non-mandated genetic/genomic testing. Please check the Plan documents for coverage limitations:

For Commercial and ASO plans please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for coverage details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination).

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM.

Where genetic/genomic testing is a benefit …
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.**

Hierarchy for genetic/genomic testing criteria

I. For **Medicare-line** members:
1. See sections V, VI, VII below using applicable Novitas-Solutions LCDs/LCAs or Palmetto GBA MolDX LCDs/LCAs
2. InterQual®

II. For **Commercial** members:
1. InterQual®

2. See sections V, VI, VII below using applicable Novitas-Solutions LCDs/LCAs or Palmetto GBA MolDX LCDs/LCAs

III. **For Medicaid plans**, please confirm coverage as outlined in the Texas Medicaid TMPPM. Then use InterQual® if further guidance is needed.

IV. If an appropriate criterion set is not found in the resources above, the request will be processed using the overarching principles that follow:

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.

V. 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.

VI. SWHP will use the following Medicare resources for both Commercial and Medicare lines:

Guidance for most codes can be found in Novitas-Solutions LCD/LCA L35396/A52986 or MolDX LCA A57503. Refer to those policies when directed to do so by items I and II at beginning of policy.

Guidance for the following codes can be found in an NCD or Palmetto GBA MolDX LCDs/LCAs as noted. Use when directed to do so by items I. and II. at beginning of policy:

0037U	FoundationOne CDx™ (F1CDx)	Coverage with criteria	IQ or NCD 90.2
0045U	Oncotype DX® Genomic Breast DISC Score	Coverage with criteria	IQ or A56887
0047U	Oncotype DX® Genomic Prostate Score	Coverage with criteria	IQ or A58371
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, algorithm reported as metastasis risk score	Limited coverage	L38303 A58371

VII. 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 (list is NOT all inclusive):

0003U	Oncology (ovarian) biochemical assays of five proteins (apolipoprotein A-1, CA 125 II, follicle	E&I Unproven

	stimulating hormone, human epididymis protein 4, transferrin), utilizing serum, algorithm reported as a likelihood score	A52986
0005U	Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score	E&I Unproven A52986
0009U	Oncology (breast cancer), ERBB2 (HER2) copy number by FISH, tumor cells from formalin fixed paraffin embedded tissue isolated using image-based dielectrophoresis (DEP) sorting, reported as ERBB2 gene amplified or non-amplified	E&I Unproven A52986
0013U	Oncology (solid organ neoplasia), gene rearrangement detection by whole genome next-generation sequencing, DNA, fresh or frozen tissue or cells, report of specific gene rearrangemen	E&I Unproven A52986
0014U	Hematology (hematolymphoid neoplasia), gene rearrangement detection by whole genome next-generation sequencing, DNA, whole blood or bone marrow, report of specific gene rearrangemen	E&I Unproven A52986
0016U	Oncology (hematolymphoid neoplasia), RNA, BCR/ABL1 major and minor breakpoint fusion transcripts, quantitative PCR amplification	E&I Unproven A52986
0017U	Oncology (hematolymphoid neoplasia), JAK2 mutation, DNA, PCR amplification of exons 12-14 and sequence analysis	E&I Unproven A52986
81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis,	E&I Unproven [eviCore]
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, P450 enzymes are involved in the hepatic metabolism of up to 50% of all clinically used drugs.	E&I Unproven [eviCore]
81422	Fetal chromosomal aneuploidy (eg, trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21	E&I Unproven
81434	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, RHO, RP1, RP2, RPE65, RPGR, and USH2A	E&I Unproven
81470	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	E&I Unproven
81471	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	E&I Unproven
81493	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	E&I Unproven L37612/A56930
81535	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 [ChemoFX]	E&I Unproven [eviCore]
81536	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) [ChemoFX]	E&I Unproven [eviCore]
81539	4Kscore test	E&I Unproven L36979

VIII. 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).

IX. Other information

Genetic Test codes with Prior Authorization (PA) diagnosis specifications:

81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed	No PA if Prenatal Dx present
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)	No PA if Prenatal Dx present
81221	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; known familial variants	No PA if Prenatal Dx present
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants	No PA if Prenatal Dx present
81223	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; full gene sequence	No PA if Prenatal Dx present
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)	No PA if Prenatal Dx present
81238	F9 (coagulation factor IX) (eg, hemophilia B)	No PA if Prenatal Dx present
81259	HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis, for common deletions or variant (eg, Southeast Asian, Thai, Filipino,	No PA if Prenatal Dx present
81302	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; full sequence analysis	No PA if Prenatal Dx present
81303	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; known familial variant	No PA if Prenatal Dx present
81304	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; duplication/deletion variants	No PA if Prenatal Dx present
81329	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis (eg, carrier testing), includes SMN2 (survival of motor neuron 2, centromeric) analysi	No PA if Prenatal Dx present
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence	No PA if Prenatal Dx present
81337	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)	No PA if Prenatal Dx present
88267	Chromosome analysis, amniotic fluid or chorionic villus, count 15 cells, 1 karyotype, with banding	No PA if Prenatal Dx present
88269	Chromosome analysis, in situ for amniotic fluid cells, count cells from 6-12 colonies, 1 karyotype, with banding	No PA if Prenatal Dx present

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.

CPT Codes:	
HCPCS Codes:	
ICD-10:	
ICD-10 Not covered:	

CMS: There is no NCD.

POLICY HISTORY:

Status	Date	Action
New	08/01/2010	New policy
Reviewed	12/06/2011	Reviewed.
Reviewed	12/06/2012	Revised. BRCA added. Criteria revised
Reviewed	11/14/2013	BRCA criteria updated.
Reviewed	04/24/2014	Minor updates made.
Reviewed	07/02/2015	Extensively re-written
Reviewed	09/08/2016	Clarified criteria; added pharmacogenetics section.
Update	06/27/2017	Updated criteria for NIPT.
Reviewed	08/22/2017	Set most testing limit to once per lifetime. Updated criteria. New request form.
Minor correction	11/28/2017	Removed discussion regarding FIT-DNA stool testing
Reviewed	06/26/2018	Significant revision of several coverage topics.
Addition	02/12/2019	InterQual® to be used instead of policy for five codes.
Major revision	09/26/2019	Policy re-written to direct reviews to InterQual®
Reviewed	05/28/2020	Redesign incorporating LCD and Palmetto GBA MolDX
Reviewed	04/22/2021	

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.

1. Calderon-Margalit R, Paltiel O. Prevention of Breast Cancer in Women Who Carry BRCA1 or BRCA2 Mutations: A Critical Review of the Literature. Int J Cancer. 2004 Nov 10;112(3):357- 64.
2. National Comprehensive Cancer Network. Practice Guidelines in Oncology. Genetic/Familial High-Risk Assessment: Breast and Ovarian. Version 1. 2006. http://www.nccn.org/professionals/physiciangls/PDF/geneticsscreening.pdf
3. National Cancer Institute. Genetics of Colorectal Cancer (PDQ®). Last Modified 03/24/2006. http://nci.nih.gov/cancertopics/pdq/genetics/colorectal/healthprofessional.
4. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Colorectal Screening. Version 1. 2006.
5. http://www.nccn.org/professionals/physician gls/PDF/colorectal screening.pdf.
6. Croitoru ME, Cleary SP, Di Nicola N, Manno M, Selander T, Aronson M, Redston M, Cotterchio M, Knight J, Gryfe R, Gallinger S. Association between biallelic and monoallelic germline MYH gene mutations and colorectal cancer risk. J Natl Cancer Inst. 2004 Nov 3;96(21):1631-4.
7. Venesio T, Molatore S, Cattaneo F, Arrigoni A, Risio M, Ranzani GN.
8. High frequency of MYH gene mutations in a subset of patients with familial adenomatous polyposis. Gastroenterology. 2004 Jun; 126(7): 1681-5.
9. Sieber OM, Lipton L, Crabtree M, Heinimann K, Fidalgo P, Phillips RK, Bisgaard ML, Orntoft TF, Aaltonen LA, Hodgson SV, Thomas HJ, Tomlinson IP. Multiple colorectal adenomas, classic adenomatous polyposis, and germ-line mutations in MYH. N Engl J Med. 2003 Feb 27;348(9):791 -9.
10. Grosse SD, Boyle CA, Botkin JR et al. Newborn Screening for Cystic Fibrosis. CDC Recommendations and Reports. October 15, 2004. http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5313a1.htm
11. Richards CS, Bradley LA, Amos J. et al. ACMG Technical Standards and Guidelines for CFTR Mutation Testing 2006 Edition. http://www.acmg.net/Pages/ACMG_Activities/stds¬2002/cf.htm
12. Moskowitz SM, Gibson RL, Sternen DL, Cheng E, Cutting GR. CFTR-Related Disorders. August 2005. Available at: www.genetests.org.
13. ACOG Committee Opinion 690, March 2017: Carrier screening in the age of genomic medicine
14. ACOG Practice Bulletin 102, March 2017 (reaffirmed 2016): Management of stillbirth
15. American College of Obstetricians and Gynecologists Committee Opinion No 691: Carrier screening for genetic conditions carrier screening for genetic conditions 2017
16. American College of Medical Genetics, Points to consider in the clinical application of genomic sequencing Genet Med 2012 Aug 14(8):759-61 Policy statement whole exome and whole genome testing
17. American College of Medical Genetics and Genomics Practice Guidelines

SWHP Genetic Testing Prior Authorization Form

6/26/2018 version

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

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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: ___/____/_____