Germline Multi-Gene Panel Testing

Policy Number: PG0453
Last Review: 5/01/2023

PARAMOUNT

HMO & PPO
MARKETPLACE
MEDICARE – ELITE, MAP

GUIDELINES

- This policy does not certify benefits or authorization of benefits, which is designated by each individual policyholder terms, conditions, exclusions and limitations contract. It does not constitute a contract or guarantee regarding coverage or reimbursement/payment. Self-Insured group specific policy will supersede this general policy when group supplementary plan document or individual plan decision directs otherwise.
- Paramount applies coding edits to all medical claims through coding logic software to evaluate the accuracy and adherence to accepted national standards.
- This medical policy is solely for guiding medical necessity and explaining correct procedure reporting used to assist in making coverage decisions and administering benefits.

SCOPE

X Professional
X Facility

DESCRIPTION

Next-generation sequencing provides the ability to analyze multiple genes simultaneously. This technology has the potential for more cost-effective testing when multiple genetic tests are indicated as well as quicker turnaround times. The specific genes included in these panels and the particular next-generation sequencing technology utilized may differ between manufacturers. As some manufacturers include genes that are less well studied, multi-gene panels can result in more complex findings.

Multi-gene panels are utilized in many areas of healthcare. Often manufacturers will curate multi-gene panels specific to a particular diagnosis. Examples of diagnoses that may be associated with multiple genes include (but are not limited to) hereditary cancer, epilepsy, hearing loss, cardiomyopathy, arrhythmias, intellectual disability, thrombophilia, and retinal dystrophy. Additionally, there are “expanded carrier screening tests” that are multi-gene panels.

POLICY

Paramount Commercial Insurance Plans and Medicare Advantage Plans

Multi-gene panel testing coverage listed below. Codes: 81410, 81411, 81412, 81413, 81414, 81415, 81416, 81417, 81418, 81419, 81425, 81426, 81427, 81430, 81431, 81432, 81433, 81434, 81435, 81436, 81437, 81438, 81439, 81440, 81441, 81442, 81443, 81448, 81460, 81465, 81470, 81471.

Medicare Advantage Plans is excluded for indications based upon family history solely.

If the servicing laboratory selects to use multiple CPT codes (i.e., unbundled or stacked version) for billing purposes, and the medical necessity criteria are met below for a panel, the laboratory will be strongly encouraged to use an applicable panel CPT code.

COVERAGE CRITERIA

Paramount Commercial Insurance Plans and Medicare Advantage Plans

Counseling
Pre-test and post-test genetic counseling is recommended when multi-gene panel testing is being offered. Documentation of pre-test genetic counseling is required for coverage of multi-gene panel testing and should detail informed consent.

Informed consent is a necessary component of pre-test counseling and should include discussion of the following topics (NSGC, 2012):

- Purpose of test and who to test (i.e., discussion of limitations to testing an unaffected individual in the absence of a known familial mutation)
- General information about gene(s) included in the testing
- Possible test results (positive, negative, uncertain findings)
- Technical aspects and accuracy of test
- Economic considerations
- Potential for genetic discrimination (i.e., discussion of the Genetic Information Non-Discrimination Act, and applicable state laws)
- Psychosocial aspects
- Confidentiality
- Utilization of test results (i.e., potential medical management options)
- Alternatives to testing

A 3-generation pedigree should be completed during pre-test counseling. The 3-generation pedigree is required for prior authorization of multi-gene panel testing.

In circumstances where the individual is unaffected but genetic testing is being considered due to family history (in the absence of a known familial mutation), further information will be required to determine medical necessity[1].

Paramount Commercial Insurance Plans

Hereditary Cancer Multi-Gene Panel Testing

- Breast/Ovarian/Pancreatic/Prostate Cancer Susceptibility: Testing for cancer susceptibility using multi-gene panels (containing 5-50 genes) is considered medically necessary when the panel contains BRCA1 and BRCA2 and an individual meets criteria for BRCA genetic testing according to Paramount Medical Policy PG0067 (Genetic Testing for Hereditary Breast and Ovarian Cancer syndrome).

- Colorectal Cancer Susceptibility: Testing for Lynch syndrome (Hereditary Non-Polyposis Colorectal Cancer) using gene panels (containing 5-50 genes) is considered medically necessary when the panel contains, at a minimum, the following genes: EPCAM, MLH1, MSH2, MSH6, and PMS2, and an individual meets criteria for Lynch syndrome genetic testing according to Paramount Medical Policy PG0302 (Genetic Testing for Lynch Syndrome and Polyposis Syndromes).

- Colorectal Cancer Susceptibility: Testing for Familial Adenomatous Polyposis (FAP) and/or MUTYH-Associated Polyposis (MAP) using gene panels (containing 5-50 genes) is considered medically necessary when the panel contains, at a minimum, the following genes: APC and MUTYH, and an individual meets criteria for genetic testing for Adenomatous Polyposis according to Paramount Medical Policy PG0302 (Genetic Testing for Lynch Syndrome and Polyposis Syndromes).

Medicare Advantage Plans
All the following must be present for coverage eligibility:

- The patient must have:
  - Any cancer diagnosis
  - AND a clinical indication for germline (inherited) testing for hereditary cancer
  - AND a risk factor for germline (inherited) cancer
  - AND has not been previously tested for the same germline genetic content.
- The test has satisfactorily completed a Technical Assessment (TA) by Molecular Diagnostic Services Program (MolDX®) for the stated indications of the test.

- The test performed includes **at least** the minimum genetic content (genes or genetic variants) with definitive or well-established guidelines-based evidence required for clinical decision making for its intended use that can be reasonably detected by the test.
    - Because these genes and variants will change as the literature and drug indications evolve, they are listed separately in associated documents, such as the MolDX® TA forms.
    - A single gene or variant may be tested if it is the only gene or variant considered to be reasonable and necessary for a cancer type.
- If a previous test was performed with a similar/duplicative intended use, a subsequent test is only reasonable and necessary if the non-duplicative genetic content of the second test is reasonable and necessary.
- If the test is an NGS test, it must abide by all conditions listed in the NCD 90.2.

Situations in which a test should not be used, or coverage is denied:

The test in question will be non-covered if:

- It is an NGS test and does not fulfill all the criteria set forth in the NCD 90.2
- A previous test was performed for the same genetic content
- It is a panel or single gene test used to identify a known familial variant(s) that could be identified with a test targeted to that specific variant(s)
- It is a panel or single gene test used to confirm a variant(s) detected by somatic tumor testing that can be confirmed by a test targeted to that specific variant(s)
- A satisfactory TA is not completed
- For tests that are currently covered but a TA submission has not been made, providers must submit complete TA materials by the original effective date of the policy or coverage will be denied

Paramount Commercial Insurance Plans and Medicare Advantage Plans

Other Medical Necessity/Indication

(Medicare Advantage Plans is excluded for indications based upon family history solely).

Germline multi-gene panels are considered medically necessary when the following criteria are met:

- The individual meets genetic testing criteria listed in previous medical policies for at least two conditions (or if there are not published medical policies for the specific condition, there are established professional guidelines that can be considered, however this needs to be documented)
- The results will directly impact the individual's medical management
- There is clinical suspicion that the condition of concern is related to a genetic etiology
- The condition of concern has multiple genes that are associated to it in which management guidelines exist

Note: The multi-gene panel policy does not apply to individuals who only meet criteria for Spinal Muscular Atrophy and Cystic Fibrosis carrier screening.

Please submit an unaffected member request for multi-gene panel genetic testing with the prior authorization request.

CODING/BILLING INFORMATION

The inclusion or exclusion of a code in this section does not necessarily indicate coverage. Codes referenced in this clinical policy are for informational purposes only.

Codes that are covered may have selection criteria that must be met.

Payment for supplies may be included in payment for other services rendered.

CPT CODES		Paramount Commercial Insurance Plans	Medicare Advantage Plans	
Genomic Sequencing Procedures and Other Molecular Multianalyte Assays (MAA)				
81410	Aortic dysfunction or dilation (e.g., Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1	**Prior Authorization required**	**Prior Authorization required**	

81411	Aortic dysfunction or dilation (e.g., Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); duplication/deletion analysis panel, must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1	**Prior Authorization required**	**Prior Authorization required**	
81412	Ashkenazi Jewish associated disorders (e.g., Bloom syndrome, Canavan disease, cystic fibrosis, familial dysautonomia, Fanconi anemia group C, Gaucher disease, Tay-Sachs disease), genomic sequence analysis panel, must include sequencing of at least 9 genes, including ASPA, BLM, CFTR, FANCC, GBA, HEXA, IKBKAP, MCOLN1, and SMPD1	**Prior Authorization required**	**Prior Authorization required**	
		PG0453 Germline Multi-Gene Panel Testing/PG0442 Carrier Screening for Genetic Diseases		
81413	Cardiac ion channelopathies (e.g., Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A	**Prior Authorization required**	**Prior Authorization required**	
		PG0453 Germline Multi-Gene Panel Testing/PG0280 Genetic Testing for Cardiac Conditions		
81414	Cardiac ion channelopathies (e.g., Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1	**Prior Authorization required**	**Prior Authorization required**	
		PG0453 Germline Multi-Gene Panel Testing/PG0280 Genetic Testing for Cardiac Conditions		
81415	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis	**Prior Authorization required**	**Non-Covered**	
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81416	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (e.g., parents, siblings) (List separately in addition to code for primary procedure)	**Prior Authorization required**	**Non-Covered**	
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81417	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (e.g., updated knowledge or unrelated condition/syndrome)	**Prior Authorization required**	**Non-Covered**	
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81418	Drug metabolism (e.g., pharmacogenomics) genomic sequence analysis panel, must include testing of at least 6 genes, including CYP2C19, CYP2D6, and CYP2D6 duplication/deletion analysis	**PG0453 Germline Multi-Gene Panel Testing/ CYP2C19 & CYP2D6 Pharmacogenetic Testing/ PG0368 Pharmacogenomic Testing for Mental Health Conditions**		
		Non-Covered	**Prior Authorization Required**	
81419	Epilepsy genomic sequence analysis panel, must include analyses for ALDH7A1,	**Prior Authorization required effective 5/1/2021**	**Prior Authorization required effective 5/1/2021**	

	CACNA1A, CDKL5, CHD2, GABRG2, GRIN2A, KCNQ2, MECP2, PCDH19, POLG, PRRT2, SCN1A, SCN1B, SCN2A, SCN8A, SLC2A1, SLC9A6, STXBP1, SYNGAP1, TCF4, TPP1, TSC1, TSC2, and ZEB2	**PG0453 Germline Multi-Gene Panel Testing/PG0467 Genetic Testing for Epilepsy**	
81425	Genome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis	**Non-Covered**	**Non-Covered**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)	
81426	Genome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (e.g., parents, siblings) (List separately in addition to code for primary procedure)	**Non-Covered**	**Non-Covered**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)	
81427	Genome (e.g., unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (e.g., updated knowledge or unrelated condition/syndrome)	**Non-Covered**	**Non-Covered**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)	
81430	Hearing loss (e.g., nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1	**Prior Authorization required**	**Prior Authorization required**
81431	Hearing loss (e.g., nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes	**Prior Authorization required**	**Prior Authorization required**
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53	**Prior Authorization required**	**Prior Authorization required**
		PG0067 Genetic Testing for Breast and Ovarian Cancers/PG0453 Germline Multi-Gene Panel Testing	
81433	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11	**Prior Authorization required**	**Prior Authorization required**
		PG0067 Genetic Testing for Breast and Ovarian Cancers/PG0453 Germline Multi-Gene Panel Testing	
81434	Hereditary retinal disorders (e.g., 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	**Prior Authorization required**	**Prior Authorization required**

81435	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include analysis of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4 and STK11	**Prior Authorization required**	**Prior Authorization required**	
		PG0302 Genetic Testing for Lynch Syndrome and Polyposis Syndromes/PG0453 Germline Multi-Gene Panel Testing		
81436	Hereditary colon cancer disorders (e.g., Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion gene analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11	**Prior Authorization required**	**Prior Authorization required**	
		PG0302 Genetic Testing for Lynch Syndrome and Polyposis Syndromes/PG0453 Germline Multi-Gene Panel Testing		
81437	Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma; genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL	**Prior Authorization required**	**Prior Authorization required**	
81438	Hereditary neuroendocrine tumor disorders (e.g., medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma; duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL	**Prior Authorization required**	**Prior Authorization required**	
81439	Hereditary cardiomyopathy (e.g., hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), genomic sequence analysis panel, must include sequencing of at least 5 cardiomyopathy-related genes (e.g., DSG2, MYBPC3, MYH7, PKP2, TTN)	**Prior Authorization required**	**Prior Authorization required**	
		PG0280 Genetic Testing for Cardiac Conditions/PG0453 Germline Multi-Gene Panel Testing		
81440	Nuclear encoded mitochondrial genes (e.g., 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	**Prior Authorization required**	**Prior Authorization required**	
81441	Inherited bone marrow failure syndromes (IBMFS) (e.g., Fanconi anemia, dyskeratosis congenita, Diamond-Blackfan anemia, Shwachman-Diamond syndrome, GATA2 deficiency syndrome, congenital amegakaryocytic thrombocytopenia) sequence analysis panel, must include sequencing of at least 30 genes, including BRCA2, BRIP1, DKC1, FANCA, FANCB,	**Prior Authorization required**	**Prior Authorization required**	

	FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, GATA1, GATA2, MPL, NHP2, NOP10, PALB2, RAD51C, RPL11, RPL35A, RPL5, RPS10, RPS19, RPS24, RPS26, RPS7, SBDS, TERT, and TINF2			
81442	Noonan spectrum disorders (e.g., Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic sequence analysis panel, must include sequencing of at least 12 genes, including BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1	**Prior Authorization required**	**Prior Authorization required**	
81443	Genetic testing for severe inherited conditions (e.g., cystic fibrosis, Ashkenazi Jewish-associated disorders [e.g., Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (e.g. ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GB1, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)	**Prior Authorization required**	**Prior Authorization required**	
81448	Hereditary peripheral neuropathies (e.g., Charcot- Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (eg, BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1)	**Prior Authorization required**	**Prior Authorization required**	
81460	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	**Prior Authorization required**	**Prior Authorization required**	
81465	Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed	**Prior Authorization required**	**Prior Authorization required**	
81470	X-linked intellectual disability (XLID) (eg, syndromic and non-syndromic XLID); genomic sequence analysis panel, must include sequencing of at least 60 genes,	**Prior Authorization required**	**Prior Authorization required**	

	including ARX, ATRX, CDKL5, FGD1, FMR1, HUWE1, IL1RAPL, KDM5C, L1CAM, MECP2, MED12, MID1, OCRL, RPS6KA3, and SLC16A2			
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	**Prior Authorization required**	**Prior Authorization required**	
Additional Medical Policy Reference: PG0041 Genetic Testing				

REVISION HISTORY EXPLANATION
ORIGINAL DATE: 10/07/2020

Date	Explanation & Changes
5/31/19	• Policy created to reflect most current clinical evidence
10/07/19	• Additional coverage clarification documentation added, *Note: The multi-gene panel policy does not apply to individuals who only meet criteria for Spinal Muscular Atrophy and Cystic Fibrosis carrier screening.*
12/02/2020	• Medical Policy placed on the new Paramount Medical Policy Format
02/26/2021	• Updated the Medical Policy to include all the Genomic Sequencing Procedures and Other Molecular Multianalyte Assays (MAA) [as is listed in medical policy PG0041 Genetic Testing] • Added new 2021 procedure 81419
10/06/2022	• Effective 10/1/2022 procedure 81420 will be covered for the Advantage product line, without a prior authorization, when the coverage criteria are met - PG0287 Non-Invasive Prenatal Screening (NIPS)/ Cell-Free DNA Screening for Fetal Aneuploidy
01/23/2023	• Paramount added the new 2023 procedure codes 81418 and 81441, effective 01/010/2023 • Paramount removed procedure codes 81420 and 81422 as this testing does not apply to this medical policy • Paramount removed procedure codes 81445, 81450, 81455 as this testing is for somatic testing, not germline testing
02/21/2023	• Medical Policy updated to reflect Medicaid coverage to Anthem as of 02/01/2023
05/01/2023	• Paramount updated Medicare coverage based upon CMS updates • Paramount added specific additional criteria for hereditary cancer multi-gene panels to the Paramount Commercial Insurance Plans • Added new 2023 codes 81418 and 81441 to the box within the medical policy Note the codes had been added to the table within the medical policy 01/23/2023 • Removed codes 81420, 81422, 81445, 81450 and 81455 from the policy box within the medical policy. Note the codes had been removed to the table within the medical policy 01/23/2023

Paramount reserves the right to review and revise our policies periodically when necessary. When there is an update, we will publish the most current policy to https://www.paramounthealthcare.com/services/providers/medical-policies/ .

REFERENCES/RESOURCES

Centers for Medicare and Medicaid Services, CMS Manual System and other CMS publications and

services

Ohio Department of Medicaid

American Medical Association, *Current Procedural Terminology (CPT®)* and associated publications and services

Centers for Medicare and Medicaid Services, Healthcare Common Procedure Coding System, HCPCS Release and Code Sets

Industry Standard Review

Hayes, Inc.

National Society of Genetic Counselors (NSGC) Practice Guideline: Risk Assessment and Genetic Counseling for Hereditary Breast and Ovarian Cancer, Volume 21, April 2012

National Comprehensive Cancer Network® (NCCN) Guidelines, Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic

National Comprehensive Cancer Network® (NCCN) Guidelines, Genetic/Familial High-Risk Assessment: Colorectal

PRIOR TO 05/01/2022

Paramount Commercial Insurance Plans, Medicare Advantage Plans, and Paramount Advantage Medicaid

Multi-gene panel testing coverage listed below, for all product lines. Codes: 81410, 81411, 81412, 81413, 81414, 81415, 81416, 81417, 81419, 81420, 81422, 81425, 81426, 81427, 81430, 81431, 81432, 81433, 81434, 81435, 81436, 81437, 81438, 81439, 81440, 81442, 81443, 81445, 81448, 81450, 81455, 81460, 81465, 81470, 81471.

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COVERAGE CRITERIA
Paramount Commercial Insurance Plans, Medicare Advantage Plans, and Paramount Advantage Medicaid

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- Purpose of test and who to test (i.e., discussion of limitations to testing an unaffected individual in the absence of a known familial mutation)
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A 3-generation pedigree should be completed during pre-test counseling. The 3-generation pedigree is required for

prior authorization of multi-gene panel testing.

In circumstances where the individual is unaffected but genetic testing is being considered due to family history (in the absence of a known familial mutation), further information will be required to determine medical necessity[1].

Paramount Commercial Insurance Plans, Medicare Advantage Plans, and Paramount Advantage Medicaid
(Medicare Advantage Plans is excluded for indications based upon family history solely).
Medical Necessity/Indication
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- The individual meets genetic testing criteria listed in previous medical policies for at least two conditions (or if there are not published medical policies for the specific condition, there are established professional guidelines that can be considered, however this needs to be documented)
- The results will directly impact the individual's medical management
- There is clinical suspicion that the condition of concern is related to a genetic etiology
- The condition of concern has multiple genes that are associated to it in which management guidelines exist

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81413	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
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81414	Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); duplication/deletion gene analysis panel, must include analysis of at least 2 genes, including KCNH2 and KCNQ1	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
		PG0453 Germline Multi-Gene Panel Testing/PG0280 Genetic Testing for Cardiac Conditions		
81415	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis	**Prior Authorization required**	**Non-Covered**	**Prior Authorization required**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81416	Exome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (eg, parents, siblings) (List separately in addition to code for primary procedure)	**Prior Authorization required**	**Non-Covered**	**Prior Authorization required**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81417	Exome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (eg, updated knowledge or unrelated condition/syndrome)	**Prior Authorization required**	**Non-Covered**	**Prior Authorization required**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81418	Drug metabolism (eg, pharmacogenomics) genomic sequence analysis panel, must include testing of at least 6 genes, including CYP2C19, CYP2D6, and CYP2D6 duplication/deletion analysis	**PG0453 Germline Multi-Gene Panel Testing/ CYP2C19 & CYP2D6 Pharmacogenetic Testing/ PG0368 Pharmacogenomic Testing for Mental Health Conditions**		
		Non-Covered	**Prior Authorization Required**	**Non-Covered**
81419	Epilepsy genomic sequence analysis panel, must include analyses for ALDH7A1, CACNA1A, CDKL5, CHD2, GABRG2, GRIN2A, KCNQ2, MECP2, PCDH19, POLG, PRRT2, SCN1A, SCN1B, SCN2A, SCN8A, SLC2A1, SLC9A6, STXBP1, SYNGAP1, TCF4, TPP1, TSC1, TSC2, and ZEB2	**Prior Authorization required effective 5/1/2021**	**Prior Authorization required effective 5/1/2021**	**Prior Authorization required effective 5/1/2021**
		PG0453 Germline Multi-Gene Panel Testing/PG0467 Genetic Testing for Epilepsy		
81425	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis	**Non-Covered**	**Non-Covered**	**Prior Authorization required**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		

81426	Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure)	**Non-Covered**	**Non-Covered**	**Prior Authorization required**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81427	Genome (eg, unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (eg, updated knowledge or unrelated condition/syndrome)	**Non-Covered**	**Non-Covered**	**Prior Authorization required**
		PG0453 Germline Multi-Gene Panel Testing/PG0468 Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS)		
81430	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); genomic sequence analysis panel, must include sequencing of at least 60 genes, including CDH23, CLRN1, GJB2, GPR98, MTRNR1, MYO7A, MYO15A, PCDH15, OTOF, SLC26A4, TMC1, TMPRSS3, USH1C, USH1G, USH2A, and WFS1	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81431	Hearing loss (eg, nonsyndromic hearing loss, Usher syndrome, Pendred syndrome); duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81432	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 10 genes, always including BRCA1, BRCA2, CDH1, MLH1, MSH2, MSH6, PALB2, PTEN, STK11, and TP53	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
		PG0067 Genetic Testing for Breast and Ovarian Cancers/PG0453 Germline Multi-Gene Panel Testing		
81433	Hereditary breast cancer-related disorders (eg, hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
		PG0067 Genetic Testing for Breast and Ovarian Cancers/PG0453 Germline Multi-Gene Panel Testing		
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	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81435	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include analysis of at least 10 genes, including APC, BMPR1A, CDH1,	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
		PG0302 Genetic Testing for Lynch Syndrome and Polyposis Syndromes/PG0453 Germline Multi-Gene Panel Testing		

	MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4 and STK11			
81436	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion gene analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
		PG0302 Genetic Testing for Lynch Syndrome and Polyposis Syndromes/PG0453 Germline Multi-Gene Panel Testing		
81437	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma; genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81438	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma; duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81439	Hereditary cardiomyopathy (eg, hypertrophic cardiomyopathy, dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy), genomic sequence analysis panel, must include sequencing of at least 5 cardiomyopathy-related genes (eg, DSG2, MYBPC3, MYH7, PKP2, TTN)	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
		PG0280 Genetic Testing for Cardiac Conditions/PG0453 Germline Multi-Gene Panel Testing		
81440	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	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81441	Inherited bone marrow failure syndromes (IBMFS) (eg, Fanconi anemia, dyskeratosis congenita, Diamond-Blackfan anemia, Shwachman-Diamond syndrome, GATA2 deficiency syndrome, congenital amegakaryocytic thrombocytopenia) sequence analysis panel, must include sequencing of at least 30 genes, including BRCA2, BRIP1, DKC1, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, GATA1, GATA2, MPL, NHP2, NOP10, PALB2, RAD51C, RPL11, RPL35A, RPL5, RPS10, RPS19, RPS24, RPS26, RPS7, SBDS, TERT, and TINF2	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**

81442	Noonan spectrum disorders (eg, Noonan syndrome, cardio-facio-cutaneous syndrome, Costello syndrome, LEOPARD syndrome, Noonan-like syndrome), genomic sequence analysis panel, must include sequencing of at least 12 genes, including BRAF, CBL, HRAS, KRAS, MAP2K1, MAP2K2, NRAS, PTPN11, RAF1, RIT1, SHOC2, and SOS1	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81443	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish-associated disorders [eg, Bloom syndrome, Canavan disease, Fanconi anemia type C, mucolipidosis type VI, Gaucher disease, Tay-Sachs disease], beta hemoglobinopathies, phenylketonuria, galactosemia), genomic sequence analysis panel, must include sequencing of at least 15 genes (eg ACADM, ARSA, ASPA, ATP7B, BCKDHA, BCKDHB, BLM, CFTR, DHCR7, FANCC, G6PC, GAA, GALT, GB1, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81448	Hereditary peripheral neuropathies (eg, Charcot- Marie-Tooth, spastic paraplegia), genomic sequence analysis panel, must include sequencing of at least 5 peripheral neuropathy-related genes (eg, BSCL2, GJB1, MFN2, MPZ, REEP1, SPAST, SPG11, SPTLC1)	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81460	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	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
81465	Whole mitochondrial genome large deletion analysis panel (eg, Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
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	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**

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	**Prior Authorization required**	**Prior Authorization required**	**Prior Authorization required**
Additional Medical Policy Reference: PG0041 Genetic Testing				