

Genetic Testing for Diagnosis of Inherited Conditions



INDEPENDENT CARE HEALTH PLAN

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Medicare Advantage Medical Coverage Policy

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Disclaimer

The Coverage Summaries are reviewed by the iCare Medicare Utilization Management Committee. Policies in this document may be modified by a member's coverage document. Clinical policy is not intended to preempt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test, or procedure over another. Clinical technology is constantly evolving, and we reserve the right to review and update this policy periodically. References to CPT® codes or other sources are for definitional purposes only and do not imply any right to reimbursement or guarantee of claims payment. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any shape or form or by any means, electronic, mechanical, photocopying or otherwise, without permission from Humana.

Related Medicare Advantage Medical/Pharmacy Coverage Policies

Amvuttra (vutrisiran)

Evrysdi (risdiplam)

Genetic Testing

Onpattro (patisiran)

Pharmacogenomics Testing

Tegsedi (inotersen)

Voxzogo (vasoritide)

Zolgensma (onasemnogene abeparvovec-xioi)

Related Documents

Please refer to [CMS website](#) for the most current applicable CMS Online Manual System (IOMs)/National Coverage Determination (NCD)/ Local Coverage Determination (LCD)/Local Coverage Article (LCA)/ Transmittals.

Genetic Testing for Diagnosis of Inherited Conditions

	Billing and Coding: MoIDX: SMPD1 Genetic Testing			
LCD	Molecular Pathology Procedures	L35000	J6, JK - National Government Services, Inc.	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI
LCA	Billing and Coding: Molecular Pathology Procedures	A56199		
	MolDX: Molecular Diagnostic Tests (MDT)	L36021		
	Billing and Coding: MoIDX: Aspartoacyclase 2 Deficiency (ASPA) Testing	A54253		
	Billing and Coding: MoIDX: BCKDHB Gene Test	A54255		
	Billing and Coding: MoIDX: BLM Gene Analysis	A54256		
	Billing and Coding: MoIDX: Fragile X	A54264		
LCD	Billing and Coding: MoIDX: GBA Genetic Testing	A54265		
LCA	Billing and Coding: MoIDX: HEXA Gene Analysis	A54268	J15 - CGS Administrators, LLC	KY, OH
	Billing and Coding: MoIDX: IKBKAP Genetic Testing	A54270		
	Billing and Coding: MoIDX: L1CAM Gene Sequencing Guidelines	A54274		
	Billing and Coding: MoIDX: MCOLN1 Genetic Testing Guidelines	A54277		
	Billing and Coding: MoIDX: MECP2 Genetic Testing	A54278		
	Billing and Coding: MoIDX: Molecular Diagnostic Tests (MDT)	A56973		

Genetic Testing for Diagnosis of Inherited Conditions

	Billing and Coding: MoIDX: SMPD1 Genetic Testing	A54285		
LCD LCA	MoIDX: Molecular Diagnostic Tests (MDT)	L35160		
	Billing and Coding: MoIDX: Aspartoacyclase 2 Deficiency (ASPA) Testing	A55088		
	Billing and Coding: MoIDX: BCKDHB Gene Test	A55099		
	Billing and Coding: MoIDX: BLM Gene Analysis	A55113		
	Billing and Coding: MoIDX: Fragile X	A55241		
	Billing and Coding: MoIDX: GBA Genetic Testing	A55243		
	Billing and Coding: MoIDX: HEXA Gene Analysis	A55255	JE - Noridian Healthcare Solutions, LLC	CA, HI, NV, American Samoa, Guam, Northern Mariana Islands
	Billing and Coding: MoIDX: IKBKAP Genetic Testing	A55612		
	Billing and Coding: MoIDX: L1CAM Gene Sequencing	A55277		
	Billing and Coding: MoIDX: MCOLN1 Genetic Testing	A55283		
	Billing and Coding: MoIDX: Molecular Diagnostic Tests (MDT)	A57526		
Billing and Coding: MoIDX: MECP2 Genetic Testing	A55285			
Billing and Coding: MoIDX: SMPD1 Genetic Testing	A55627			
	MoIDX: Molecular Diagnostic Tests (MDT)	L36256		

LCD LCA	Billing and Coding: MoIDX: Aspartoacyclase 2 Deficiency (ASPA) Testing	A55089	JF - Noridian Healthcare Solutions, LLC	AK, AZ, ID, MT, ND, OR, SD, UT, WA, WY
	Billing and Coding: MoIDX: BCKDHB Gene Test	A55100		
	Billing and Coding: MoIDX: BLM Gene Analysis	A55114		
	Billing and Coding: MoIDX: Fragile X	A55242		
	Billing and Coding: MoIDX: GBA Genetic Testing	A55244		
	Billing and Coding: MoIDX: HEXA Gene Analysis	A55256		
	Billing and Coding: MoIDX: IKBKAP Genetic Testing	A55613		
	Billing and Coding: MoIDX: L1CAM Gene Sequencing	A55278		
	Billing and Coding: MoIDX: MCOLN1 Genetic Testing	A55284		
	Billing and Coding: MoIDX: MECP2 Genetic Testing	A55286		
Billing and Coding: MoIDX: Molecular Diagnostic Tests (MDT)	A57527			
Billing and Coding: MoIDX: SMPD1 Genetic Testing	A55631			
	MoIDX: Molecular Diagnostic Tests (MDT)	L35025		
	Billing and Coding: MoIDX: Aspartoacyclase 2 Deficiency(ASPA) Testing	A53602 A53600		

LCD LCA	Billing and Coding: MoIDX: BCKDHB Gene Test Billing and Coding: MoIDX: BLM Gene Analysis Billing and Coding: MoIDX: Fragile X Billing and Coding: MoIDX: GBA Genetic Testing Billing and Coding: MoIDX: HEXA Gene Analysis Billing and Coding: MoIDX: IKBKAP Genetic Testing Billing and Coding: MoIDX: L1CAM Gene Sequencing Billing and Coding: MoIDX: MCOLN1 Genetic Testing Billing and Coding: MoIDX: MECP2 Genetic Billing and Coding: MoIDX: Molecular Diagnostic Tests (MDT) Billing and Coding: MoIDX: SMPD1 Genetic Testing	A53540 A53638 A53542 A53598 A53596 A53659 A53630 A53574 A56853 A53624	JJ, JM - Palmetto GBA	AL, GA, NC, SC, TN, VA, WV
LCD	Molecular Pathology Procedures	L34519	JN - First Coast Service Options, Inc.	FL, PR, U.S. VI

Description

Genetic testing may be performed to analyze an individual's deoxyribonucleic acid (DNA) to detect gene variants to assist in confirming a diagnosis in those who exhibit disease signs and symptoms and to aid with treatment decisions. Examples of genetic conditions that may be evaluated by genetic testing include, but are not limited to, achondroplasia, alpha-1 antitrypsin deficiency, cardiofaciocutaneous syndrome, Celiac

disease, Charcot-Marie-Tooth disease, dystrophic epidermolysis bullosa, hereditary neuropathy with liability to pressure palsies (HNPP), muscular dystrophy, neurofibromatosis, Noonan syndrome, polycystic kidney disease (PKD) and spastic paraplegia.

Coverage Determination

iCare follows the CMS requirements that only allows coverage and payment for services that are reasonable and necessary for the diagnosis and treatment of illness or injury or to improve the functioning of a malformed body member except as specifically allowed by Medicare.

Genetic tests must demonstrate clinical utility, analytical and clinical validity and fulfill the CMS “reasonable and necessary” criteria. Analytic validity (test accurately identifies the gene variant), clinical validity (test identifies or predicts the clinically defined disorder) and clinical utility (test measurably improves clinical outcomes) of the genetic test is supported by generally accepted standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, specialty society recommendations, and views of physicians practicing in relevant clinical areas. The test must be ordered by a physician who is treating the beneficiary and the results will be used in the management of a beneficiary’s specific medical problem.

For jurisdictions with no Medicare guidance for a particular test, iCare will utilize the [MoIDX program](#) and Technical Assessments for molecular assays as the standard to evaluate clinical utility, analytical and clinical validity in conjunction with adhering to Medicare’s reasonable and necessary requirement.

In interpreting or supplementing the criteria above and in order to determine medical necessity consistently, iCare may consider the following criteria:

General Criteria for Genetic Testing for Diagnosis of Inherited Conditions

Apply General Criteria for Genetic Testing for Diagnosis of Inherited Conditions when disease- or gene-specific criteria are not available on this medical coverage policy.

Genetic testing for diagnosis of inherited conditions will be considered medically reasonable and necessary when the following requirements are met:

- Analytic validity, clinical validity and clinical utility of the genetic test is supported by the [MoIDX program](#); **AND**
- Individual displays signs and symptoms of a hereditary disease
- Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or results are clearly equivocal; **AND**
- Results of the genetic testing must directly impact treatment or management of the Medicare beneficiary

- Scientific literature reliably supports a gene-disease association

Criteria for Specific Inherited Conditions

Achondroplasia single gene testing (*FGFR3*) will be considered medically reasonable and necessary when the following requirements are met:^{83,122,147,159,184,216}

- Genetic testing is limited to the *FGFR3* gene; **AND**
- Epiphyses are confirmed open by diagnostic imaging; **AND**
- Testing will impact management of the individual (eg, vosoritide [Voxzogo])

Alpha-1 antitrypsin deficiency single gene testing (*SERPINA1*) (81332) will be considered medically reasonable and necessary for the following indications:^{16,80,123,137,138,165,187,215,221}

- Genetic testing is limited to the *SERPINA1* gene; **AND**
 - Chronic obstructive pulmonary disease (COPD); **OR**
 - Granulomatosis with polyangiitis; **OR**
 - Necrotizing panniculitis; **OR**
 - Unexplained bronchiectasis; **OR**
 - Unexplained chronic liver disease

Celiac disease *HLA-DQ2/HLA-DQ8* testing will be considered medically reasonable and necessary for the workup of an individual with an unclear diagnosis of celiac disease and gluten hypersensitivity usually related to ambiguous standard laboratory results and/or inconsistent biopsy results (eg, HLA-DQ2 by HLA-DQB1*02 and of DQ8 by HLA-DQB1*0302).⁸⁰

Dystrophic epidermolysis bullosa (DEB) single gene testing (*COL7A1*) will be considered medically reasonable and necessary when the following requirements are met:^{117,146,191}

- Genetic testing is limited to the *COL7A1* gene; **AND**
- Individual to be tested exhibits clinical characteristics of dystrophic epidermolysis bullosa (DEB) (eg, fragility of the skin, blistering and erosions, dystrophic or absent nails).

Epilepsy genomic sequence analysis multigene panel (81419) will be considered medically reasonable and necessary for unexplained epilepsy when the following requirements are met:^{68,210}

- Analytic validity, clinical validity and clinical utility of the genetic test is supported by the [MoIDX program](#); **AND**

- Alternative laboratory or clinical tests to definitively diagnose the disorder/identify the condition are unavailable or results are clearly equivocal; **AND**
- Results of the genetic testing must directly impact treatment or management of the Medicare beneficiary

Hereditary transthyretin amyloidosis single gene testing (*TTR*) will be considered medically reasonable and necessary when the following requirements are met:^{1,2,99,124,133,145,149,158,196,229,238}

- Genetic testing is limited to the *TTR* gene; **AND**
- Individual to be tested diagnosed with polyneuropathy and a comprehensive neurologic examination has ruled out other causes of sensorimotor/autonomic neuropathy (eg, chronic inflammatory demyelinating polyneuropathy); **AND**
- No history of liver transplant; **AND**
- [Polyneuropathy disability \(PND\) scoring system](#) indicates stage I, II, IIIa or IIIb; **AND**
- Testing will result in a change of management (eg, vutrisiran [Amvuttra], patisiran [Onpattro] or inotersen [Tegsedi])

Inherited retinal disorders [single gene](#)* (*ABCA4, CNGA1, CRB1, EYS, PDE6A, PDE6B, PRPF31, PRPH2, RDH12, RHO, RP1, RP2, RPE65, RPRGR, USH2A*) will be considered medically reasonable and necessary when the following requirements are met:^{4,100,129,197}

- Individual to be tested diagnosed with an inherited retinal disorder (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy); **AND**
- Exhibits progressive loss of photoreceptor function accompanied by vision loss

*For multigene panels for inherited retinal disorders, please refer to [Limitations](#).

Oculopharyngeal muscular dystrophy (OPMD) single gene testing (*PABPN1*) (81312) will be considered medically reasonable and necessary when the following requirements are met:^{68,156,205,237}

- Genetic testing is limited to the *PABPN1* gene; **AND**
- Individual to be tested has dysphagia (defined as a swallowing time greater than 7 seconds when drinking 80mL of ice-cold water as documented by a swallow study); **AND**
 - Previous corrective surgery for ptosis; **OR**

- Vertical separation of at least one palpebral fissure that measures less than 8mm at rest

Testing Strategy for OPMD: *PABPN1* gene sequence analysis or targeted analysis for GCN repeat number in exon 1.

Polycystic kidney disease (PKD) (autosomal dominant or autosomal recessive) gene testing (*PKD1*, *PKD2*, *PKHD1*) will be considered medically reasonable and necessary when the following requirements are met:^{84,85,125,160,206,207,217}

- Single gene analysis of *PKD1*, *PKD2* or *PKHD1* when the individual to be tested has equivocal or uninformative imaging results; **OR**
- Multigene panel that includes *PKD1*, *PKD2*, *PKHD1* will be considered medically reasonable and necessary when the individual to be tested has equivocal or uninformative imaging results and the analytic validity, clinical validity and clinical utility of the genetic test is supported by the [MolDX program](#).

The use of the criteria in this Medicare Advantage Medical Coverage Policy provides clinical benefits highly likely to outweigh any clinical harms. Services that do not meet the criteria above are not medically necessary and thus do not provide a clinical benefit. Medically unnecessary services carry risks of adverse outcomes and may interfere with the pursuit of other treatments which have demonstrated efficacy.

Coverage Limitations

[US Government Publishing Office. Electronic code of federal regulations: part 411 – 42 CFR § 411.15 - Particular services excluded from coverage](#)

The following tests may not be considered a benefit (statutory exclusion):

- Gaucher disease (*GBA*)^{39,40,41,42}
- Familial dysautonomia (*IKBKAP*)^{48,49,50,51,52}
- L1 syndrome (*L1CAM*)^{53,54,55,56,57}
- Maple syrup urine disease (*BCKDHB*)^{22,23,24,25,26,27}
- Mucopolysaccharidosis type IV (*MCOLN1*)^{58,59,60,61,62}
- Niemann-Pick disease (*SMPD1*)^{69,70,71,72,73}
- Tests considered screening in the absence of clinical signs and symptoms of disease that are not specifically identified by the law;²¹⁴ **OR**

- Tests that confirm a diagnosis or known information;²¹⁴ **OR**
- Tests to determine risk for developing a disease or condition;²¹⁴ **OR**
- Tests performed to measure the quality of a process;²¹⁴ **OR**
- Tests without diagnosis specific indications;²¹⁴ **OR**
- Tests identified as investigational by available literature and/or the literature supplied by the developer and are not a part of a clinical trial²¹⁴

These treatments and services fall within the Medicare program's statutory exclusion that prohibits payment for items and services that have not been demonstrated to be reasonable and necessary for the diagnosis and treatment of illness or injury (§1862(a)(1) of the Act). Other services/items fall within the Medicare program's statutory exclusion at 1862(a)(12), which prohibits payment.

The following items will not be considered medically reasonable and necessary:

- Any laboratory test that investigates the same germline genetic content, for the same genetic information, that has already been tested in the same individual
- Deletion/duplication information is obtained as part of the sequencing procedure but submitted as an independent analysis
- Genetic tests that have not demonstrated clinical utility, analytical and clinical validity via the [MoIDX Program](#)
- Bloom disease (*BLM*) (81209)^{28,29,30,31,32}
- Canavan disease (also known as asparoacylase 2 deficiency [*ASPA*])^{17,18,19,20,21}
- Charcot-Marie-Tooth for any of the following genes:
 - *GJB1*⁸⁰
 - *MPZ*⁸⁰
 - *PMP22* full gene sequencing (81325)⁶⁸
 - *PMP22* deletion/duplication analysis (81324)⁶⁸
 - *PMP22* known familial variant analysis (81326)⁶⁸
- Corneal dystrophy (*TGFB1*) (81333)⁶⁸
- Duchenne/Becker muscular dystrophy (*DMD*) (81161/0218U)⁶⁸
- Fragile X syndrome (*FMR1* [81243/81244] and *AFF2* [81171/81172] genes)^{33,34,35,36,37}

- Hereditary peripheral neuropathies genomic sequence analysis panel (81448)⁶⁸
- Inherited retinal disorders (eg, retinitis pigmentosa, Leber congenital amaurosis, cone-rod dystrophy) genomic sequence analysis panel (81434)⁶⁸
- Myotonic dystrophy type 1 - *DMPK* full gene sequence analysis (81187)⁶⁸
- Myotonic dystrophy type 2 (*CNBP*) (81234/81239)⁶⁸
- Neurofibromatosis type 1 single gene testing (*NF1*)⁸⁰
- NF2-related schwannomatosis (formerly neurofibromatosis type 2) single gene testing (*NF2*)⁸⁰
- Nonsyndromic hearing loss including the following:
 - Genomic sequence analysis panel (81430) and deletion/duplication analysis panel (81431)⁶⁸
 - *GJB2* (81252/81253)⁶⁸
 - *GJB6* (81254)⁶⁸
- Noonan spectrum disorders including the following:
 - Genomic sequence analysis panel (81442)⁶⁸
 - *PTPN11*⁸⁰
 - *SOS1*⁸⁰
- Prader-Willi syndrome (*UBE3A*) (81331)⁸⁰
- Rett syndrome (*MECP2* [81302/81304/0234U])^{63,64,65,66,67}
- Spinal and bulbar muscular atrophy (Kennedy's Disease) (*AR*) (81204/81173/81174/0230U)⁸⁰
- Spinal muscular atrophy (*SMN1*) (81336)⁸⁰
- Tay-Sachs disease (*HEXA*)^{43,44,45,46,47}
- X-linked intellectual disability (XLID) genomic sequence analysis panel (81470) and deletion/duplication analysis panel (81471)⁶⁸

A review of the current medical literature shows that the evidence is insufficient to determine that these services are standard medical treatments. There remains an absence of randomized, blinded clinical studies examining benefit and long-term clinical outcomes establishing the value of these services in clinical management.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed	
81171	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	
81172	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; characterization of alleles (eg, expanded size and methylation status)	
81173	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence	
81174	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant	
81187	CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81188	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	
81189	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; full gene sequence	
81190	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; known familial variant(s)	
81200	ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)	
81204	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; characterization of alleles (eg, expanded size or methylation status)	
81205	BCKDHB (branched-chain keto acid dehydrogenase E1, beta polypeptide) (eg, maple syrup urine disease) gene analysis, common variants (eg, R183P, G278S, E422X)	

81209	BLM (Bloom syndrome, RecQ helicase-like) (eg, Bloom syndrome) gene analysis, 2281del6ins7 variant	
81234	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles	
81239	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)	
81242	FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia, type C) gene analysis, common variant (eg, IVS4+4A>T)	
81243	FMR1 (fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal (eg, expanded) alleles	
81244	FMR1 (fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and promoter methylation status)	
81250	G6PC (glucose-6-phosphatase, catalytic subunit) (eg, Glycogen storage disease, type 1a, von Gierke disease) gene analysis, common variants (eg, R83C, Q347X)	
81251	GBA (glucosidase, beta, acid) (eg, Gaucher disease) gene analysis, common variants (eg, N370S, 84GG, L444P, IVS2+1G>A)	
81252	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; full gene sequence	
81253	GJB2 (gap junction protein, beta 2, 26kDa, connexin 26) (eg, nonsyndromic hearing loss) gene analysis; known familial variants	
81254	GJB6 (gap junction protein, beta 6, 30kDa, connexin 30) (eg, nonsyndromic hearing loss) gene analysis, common variants (eg, 309kb [del(GJB6-D13S1830)] and 232kb [del(GJB6-D13S1854)])	
81255	HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)	
81260	IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (eg, familial dysautonomia) gene analysis, common variants (eg, 2507+6T>C, R696P)	
81290	MCOLN1 (mucolipin 1) (eg, Mucopolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)	
81302	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; full sequence analysis	

81303	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; known familial variant	
81304	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome) gene analysis; duplication/deletion variants	
81312	PABPN1 (poly[A] binding protein nuclear 1) (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles	
81324	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; duplication/deletion analysis	
81325	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; full sequence analysis	
81326	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant	
81330	SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)	
81331	SNRPN/UBE3A (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis	
81332	SERPINA1 (serpin peptidase inhibitor, clade A, alpha-1 antiproteinase, antitrypsin, member 1) (eg, alpha-1-antitrypsin deficiency), gene analysis, common variants (eg, *S and *Z)	
81333	TGFBI (transforming growth factor beta-induced) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)	
81336	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence	
81377	HLA Class II typing, low resolution (eg, antigen equivalents); one antigen equivalent, each	
81382	HLA Class II typing, high resolution (ie, alleles or allele groups); one locus (eg, HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each	
81383	HLA Class II typing, high resolution (ie, alleles or allele groups); one allele or allele group (eg, HLA-DQB1*06:02P), each	
81403	MOLECULAR PATHOLOGY PROCEDURE LEVEL 4	
81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5	
81405	MOLECULAR PATHOLOGY PROCEDURE LEVEL 6	

81406	MOLECULAR PATHOLOGY PROCEDURE LEVEL 7	
81407	MOLECULAR PATHOLOGY PROCEDURE LEVEL 8	
81408	MOLECULAR PATHOLOGY PROCEDURE LEVEL 9	
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	
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	
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	
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	
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	
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)	
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	

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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	
81479	Unlisted molecular pathology procedure	
0218U	Neurology (muscular dystrophy), DMD gene sequence analysis, including small sequence changes, deletions, duplications, and variants in non-uniquely mappable regions, blood or saliva, identification and characterization of genetic variants	
0230U	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation), full sequence analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions	
0232U	CSTB (cystatin B) (eg, progressive myoclonic epilepsy type 1A, Unverricht-Lundborg disease), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, short tandem repeat (STR) expansions, mobile element insertions, and variants in non-uniquely mappable regions	
0234U	MECP2 (methyl CpG binding protein 2) (eg, Rett syndrome), full gene analysis, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions	
0236U	SMN1 (survival of motor neuron 1, telomeric) and SMN2 (survival of motor neuron 2, centromeric) (eg, spinal muscular atrophy) full gene analysis, including small sequence changes in exonic and intronic regions, duplications, deletions, and mobile element insertions	
CPT® Category III Code(s)	Description	Comments
No code(s) identified		
HCPCS Code(s)	Description	Comments
No code(s) identified		

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Appendix

Appendix A

Family Relationships

Degree of Relationship	Relative of the Individual to be Tested
First-degree	Child, full-sibling, parent
Second-degree	Aunt, uncle, grandchild, grandparent, nephew, niece, half-sibling
Third-degree	First cousin, great aunt, great-uncle, great-grandchild, great-grandparent, half-aunt, half-uncle

Appendix B

Polyneuropathy Disability (PND) Scoring System¹³³

Stage	Description
0	No symptoms of neuropathy
I	Sensory disturbance but with preserved walking capacity
II	Unassisted walking but with difficulty
IIIa	One stick or crutch is required for walking
IIIb	Two sticks or crutches are required for walking
IV	Wheelchair-bound or bedridden

Change Summary

- 01/01/2024 New Policy.