Centers for Medicare and Medicaid Services

Clinical Laboratory Fee Schedule
Annual Laboratory Public Meeting

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Anthony Sireci, MD, Msc

Association for Molecular Pathology

Outline

- Germline Procedures
  - Triplet Repeat Disorders Procedures - Evaluation of abnormal alleles (8X001, 8X003, 8X006-8X013, 8X016, 8X017, 8X020, 8X022, 8X026, 8X028, 8X035, 8X036)
  - Triplet Repeat Disorders Procedures - Characterization of alleles (8X002, 8X021, 8X023, 8X027)
  - Full Gene Sequence Procedures (non-BRCA) (8X004, 8X014, 8X018, 8X024, 8X033)
  - Familial Variant Detection Procedures (non-BRCA) (8X005, 8X015, 8X019, 8X025, 8X034)
  - Common Variant Detection Procedures (non-BRCA) (8X000, 813X0, 8X032)
  - BRCA Procedures (81X78, 81X79, 81X81, 81X82, 81X83)
- Oncology-related Procedures
  - Common Variants or Targeted Sequencing Procedures (81X08-81X11, 80X00)
  - Full Gene Sequence Procedures (81X07)
- Genomic Sequencing Procedure (81X43)
- Reconsidered Procedures (81334 and 81326)

Basis for Crosswalk Recommendations

- Analysis of:
  - Analytical methods employed
  - Overall resources utilized
  - Types of genetic variants tested (e.g., SNPs, deletions, etc.,.)
  - Amount of genetic material interrogated

Background: Triplet Repeat Disorders – Evaluation of Abnormal Alleles 8X001, 8X003, 8X006-8X013, 8X016, 8X017, 8X020, 8X022, 8X026, 8X028, 8X035, 8X036

New Code	Descriptor
8X001	AFF2 (AF4/FMR2 family, member 2 [FMR2]) (eg, fragile X mental retardation 2 [FRAXE]) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
8X003	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)
8X006	ATN1 (atrophin 1) (eg, dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X007	ATXN1 (ataxin 1) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X008	ATXN10 (ataxin 10) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X009	ATXN2 (ataxin 2) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X010	ATXN3 (ataxin 3) (eg, spinocerebellar ataxia, Machado-Joseph disease) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X011	ATXN7 (ataxin 7) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X012	ATXN8OS (ATXN8 opposite strand [non-protein coding]) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X013	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
8X016	CNBP (CCHC-type zinc finger nucleic acid binding protein) (eg, myotonic dystrophy type 2) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X017	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
8X020	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; evaluation to detect abnormal (expanded) alleles
8X022	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; evaluation to detect abnormal (expanded) alleles
8X026	HTT (huntingtin) (eg, Huntington disease) gene analysis; evaluation to detect abnormal (eg, expanded) alleles
8X028	PABPN1 (poly[A] binding protein nuclear 1) (eg, oculopharyngeal muscular dystrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X035	PPP2R2B (protein phosphatase 2 regulatory subunit Bbeta) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
8X036	TBP (TATA box binding protein) (eg, spinocerebellar ataxia) gene analysis, evaluation to detect abnormal (eg, expanded) alleles

Test Purpose and Method: Triplet Repeat Disorders- Procedures Evaluation of Abnormal Alleles
8X001, 8X003, 8X006-8X013, 8X016, 8X017, 8X020, 8X022, 8X026, 8X028, 8X035, 8X036

Purpose: To aid in the diagnosis of a triplet repeat disorder.

Method: Repeat primed PCR with capillary electrophoresis

Crosswalk Recommendations: Triplet Repeat Disorders Procedures – Evaluation of Abnormal Alleles - 8X001, 8X003, 8X006-8X013, 8X016, 8X017, 8X020, 8X022, 8X026, 8X028, 8X035, 8X036

New Code	Gene Name	Public Comment	Rationale
8X001	AFF2	81401 – Molecular Pathology Procedure Level 2 ($137.00)	The methodology and amount of work used to detect triplet repeat expansion disorders is identical to that described by the Tier 2, level 2 code (81401), which is how these procedures were originally coded.
8X003	AR		
8X006	ATN1		
8X007	ATXN1		
8X008	ATXN10		
8X009	ATXN2		
8X010	ATXN3		
8X011	ATXN7		
8X012	ATXN8OS		
8X013	CACNA1A		
8X016	CNBP		
8X017	CSTB		
8X020	DMPK		
8X022	FXN		
8X026	HTT		
8X028	PABPN1		
8X035	PPP2R2B		
8X036	TBP		

Background: Triplet Repeat Disorders – Characterization of Alleles 8X002, 8X021, 8X023, 8X027

New Code	Descriptor
8X002	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)
8X021	DMPK (DM1 protein kinase) (eg, myotonic dystrophy type 1) gene analysis; characterization of alleles (eg, expanded size)
8X023	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; characterization of alleles (eg, expanded size)
8X027	HTT (huntingtin) (eg, Huntington disease) gene analysis; characterization of alleles (eg, expanded size)

Test Purpose and Method: Triplet Repeat Disorders Procedures Characterization of Alleles
8X002, 8X021, 8X023, 8X027

Purpose: To aid in the diagnosis of a triplet repeat disorder.

Method: Southern Blot

Crosswalk Recommendations: Triplet Repeat Disorders Procedures – Characterization of Alleles 8X002, 8X021, 8X023, 8X027

New Code	Gene Name	Public Comment	Rationale
8X002	AFF2	81404 – Molecular Pathology Procedure, Level 5 ($274. 83)	The methodology and amount of work used to characterize the size of the triplet repeat expansion is identical to that described by the Tier 2, Level 5 code, which is how these procedures were previously coded.
8X021	DMPK		
8X023	FXN		
8X027	HTT		

Background: Germline Full Gene Sequence Procedures (non-BRCA) – 8X004, 8X014, 8X018, 8X024, 8X033)

New Code	Descriptor
8X004	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; full gene sequence
8X014	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; full gene sequence
8X018	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; full gene sequence
8X024	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; full gene sequence
8X033	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; full gene sequence

Test Purpose and Method: Germline Full Gene Sequence Procedures (non-BRCA) – 8X004, 8X014, 8X018, 8X024, 8X033)

Purpose: To detect variants (e.g., SNVs, indels) within the entire gene.

Method: Bi-directional sequencing of coding regions as well as exon-intron junctions by Sanger sequencing or next generation sequencing.

Crosswalk Recommendations: Germline Full Gene Sequence Procedures (non-BRCA) – 8X004, 8X014, 8X018, 8X024, 8X033

New Code	Gene Name	Public Comment	Rationale
8X004	AR	81405 – Molecular Pathology Procedure, Level 6 ($301.35)	Methods used for sequencing analysis and the amount of DNA sequenced are comparable to that of 81405, which is how this procedure was previously coded.
8X014	CACNA1A	81407- Molecular Pathology Procedure, Level 8 ($846.27)	Methods used for sequencing analysis and the amount of DNA sequenced are comparable to that of 81407, which is how this procedure was previously coded.
8X018	CSTB	81404 – Molecular Pathology Procedure, Level 5 ($274.83)	Methods used for sequencing analysis and the amount of DNA sequenced are comparable to that of 81404, which is how this procedure was previously coded.
8X024	FXN	81404 – Molecular Pathology Procedure, Level 5 ($274.83)	Methods used for sequencing analysis and the amount of DNA sequenced are comparable to that of 81404, which is how this procedure was previously coded.
8X033	SMN1	81317 - PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis ($707.02)	Similar methodologies and resources are used in the full sequencing of SMN1 and PMS2.

Background: Germline Familial Variant Detection Procedures (non-BRCA) – 8X005, 8X015, 8X019, 8X025, 8X034

New Code	Descriptor
8X005	AR (androgen receptor) (eg, spinal and bulbar muscular atrophy, Kennedy disease, X chromosome inactivation) gene analysis; known familial variant
8X015	CACNA1A (calcium voltage-gated channel subunit alpha1 A) (eg, spinocerebellar ataxia) gene analysis; known familial variant
8X019	CSTB (cystatin B) (eg, Unverricht-Lundborg disease) gene analysis; known familial variant(s)
8X025	FXN (frataxin) (eg, Friedreich ataxia) gene analysis; known familial variant(s)
8X034	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; known familial sequence variant(s)

Test Purpose and Method: Germline Familial Variant Detection Procedures (non-BRCA) – 8X005, 8X015, 8X019, 8X025, 8X034

Purpose: To detect specific known variant(s) in a gene.

Method: PCR amplification followed by a targeted genotyping method (e.g., Sanger Sequencing)

Crosswalk Recommendations: Germline Familial Variant Detection Procedures (non-BRCA) – 8X005, 8X015, 8X019, 8X025, 8X034

New Code	Gene Name	Public Comment	Rationale
8X005	AR	81403 – Molecular Pathology Procedure, Level 4 ($185.20)	Methods used for sequencing analysis and the amount of DNA sequenced are comparable to that of 81403, which is how this procedure was previously coded.
8X015	CACNA1A		
8X019	CSTB		
8X025	FXN		
8X034	SMN1		

Background, Test Purpose and Method: Germline Common Variant Detection Procedures (non-BRCA) – 8X000, 813X0, 8X032

New Code	Descriptor
8X000	NUDT15 (nudix hydrolase 15) (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *3, *4, *5, *6)
813X0	TGFBI (transforming growth factor beta-induced) (eg, corneal dystrophy) gene analysis, common variants (eg, R124H, R124C, R124L, R555W, R555Q)
8X032	SMN1 (survival of motor neuron 1, telomeric) (eg, spinal muscular atrophy) gene analysis; dosage/deletion analysis, includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed

Purpose: To detect specific, common variant(s) in a gene.

Method:
8X000 and 812X0: PCR amplification followed by a targeted genotyping method (e.g., Sanger Sequencing)
8X032: Multiplexed Ligation-dependent Probe Amplification (MLPA) or delta delta CT

Crosswalk Recommendation: Germline Common Variant Detection Procedures (non-BRCA) – 8X000, 813X0, 8X032

New Code	Gene Name	Public Comment	Rationale
8X000	NUDT15	81225 - CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17) ($291.36)	Similar methodologies and resources are used to detect a comparable number of known variants in 81225
813X0	TGFBI	81230 - CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22) ($174.81)	Similar methodologies and resources are used to detect a comparable number of known variants in 81230
8X032	SMN1/2	81401 – Molecular Pathology Procedures, Level 2 ($137.00)	The methodology and amount of work used is identical to that described by the Tier 2, level 2 code which is how this procedure was previously coded

Background: BRCA Procedures – 81X78, 81X79, 81X81, 81X82, 81X83

New Code	Descriptor
81X78	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81X79	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81X81	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81X82	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81X83	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)

Test Purpose and Method: BRCA Procedures – 81X78, 81X79, 81X81, 81X82, 81X83

Purpose: To detect variants (e.g., SNVs and small indels) within one or both BRCA genes in their entirety

Method:

- **Full gene sequencing:** Bi-directional sequencing of coding regions as well as exon-intron junctions by Sanger sequencing or next generation sequencing
- **Del/Dup analysis:** Generally Multiplexed Ligation-dependent Probe Amplification (MLPA)

Crosswalk Recommendations: BRCA Procedures – 81X78, 81X79, 81X81, 81X82, 81X83

New Code	Gene Name	Public Comment	Rationale
81X78	BRCA1, BRCA2 full sequence analysis	81408 – DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy), full gene sequence; Molecular Pathology Procedure, Level 9 ($2,000.00)	The methodology and amount of DNA sequenced is comparable to the sequencing of the large gene DMD.
81X79	BRCA1, BRCA2 full duplication/deletion analysis	81213 - BRCA1, BRCA2 (breast cancer 1 and 2) (eg, hereditary breast and ovarian cancer) gene analysis; uncommon duplication/deletion variants ($553.00)	The methodology used for detection of Dup/Dels is the same as the previously used code for BRCA1/2 Dup/del uncommon analysis.
81X81	BRCA1 full sequence analysis	81408 x0.5 ($2,000.00 X 0.5 = $1,000.00)	The methodology and amount of DNA sequenced is comparable to half that of the sequencing of the large gene DMD.
81X82	BRCA1 full duplication/deletion analysis	81213 x0.5 ($553.00 X0.5= $276.5)	The methodology used for detection of Dup/Del analysis is half that as the previously used code for BRCA1/2 Dup/del uncommon analysis.
81X83	BRCA2 full duplication/deletion analysis	81213 x0.5 ($553.00 X0.5= $276.5)	The methodology used for detection of Dup/Del analysis is half that as the previously used code for BRCA1/2 Dup/del uncommon analysis.

Background: Oncology-related Procedures- Common Variants or Targeted Sequencing Procedures (81X08-81X11, 80X00)

New Code	Descriptor
81X08	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, diffuse large B-cell lymphoma) gene analysis, common variant(s) (eg, codon 646)
81X09	BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F)
81X10	PLCG2 (phospholipase C gamma 2) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, R665W, S707F, L845F)
81X11	MYD88 (myeloid differentiation primary response 88) (eg, Waldenstrom’s macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant
80X00	TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region)

Test Purpose and Method: Oncology-related Procedures- Common Variants or Targeted Sequencing Procedures (81X08-81X11, 80X00)

Purpose: To detect common variant(s) in a gene or gene promoter region.

Method: PCR amplification followed by a targeted genotyping method (e.g., Sanger Sequencing)

Crosswalk Recommendations: Oncology-related Procedures- Common Variants Or Targeted Sequencing Procedures (81X08-81X11, 80X00)

New Code	Gene Name	Public Comment	Rationale
81X08	EZH2	81210 - BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s) ($175.40)	Assessment of a single codon, hotspot variant. Similar methodologies are employed to detect variants at V600 in BRAF (81210)
81X09	BTK	81210 - BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s) ($175.40)	Assessment of a single codon, hotspot variant. Similar methodologies are employed to detect variants at V600 in BRAF (81210)
81X10	PLCG2	81225- CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17) ($291.36)	Similar methodologies and resources are used in the assessment of 3 distant codons compared to 5 common variants in 81225.
81X11	MYD88	81210 - BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s) ($175.40)	Assessment of a single codon, hotspot variant. Similar methodologies are employed to detect variants at V600 in BRAF (81210)
80X00	TERT	81121- IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (eg, glioma), common variants (eg, R140W, R172M) ($295.79)	Similar methodologies and resources are used to determine the genotype at two distant codons in IDH2.

Background and Test Purpose and Methods: Oncology-related Procedures- Full Gene Sequence Procedures (81X07)

New Code	Descriptor
81X07	EZH2 (enhancer of zeste 2 polycomb repressive complex 2 subunit) (eg, myelodysplastic syndrome, myeloproliferative neoplasms) gene analysis, full gene sequence

Test Purpose:
81X07: To detect variants (SNV and small indels) in the entire EZH2 gene in cancer or precancer

Method:
81X07: PCR amplification follow by Sanger sequencing or next generation sequencing.

Crosswalk Recommendations: Oncology-related Procedures- Full Gene Sequence Procedures (81X07)

New Code	Gene Name	Public Comment	Rationale
81X07	EZH2	81175 - ASXL1 (additional sex combs like 1, transcriptional regulator) (eg, myelodysplastic syndrome, myeloproliferative neoplasms, chronic myelomonocytic leukemia), gene analysis; full gene sequence ($707.00)	The methodology and amount of DNA sequenced is comparable to the sequencing of ASXL1, which is also relevant in hematologic malignancy.

Background and Test Purpose and Methods: Genomic Sequencing Procedure 81X43

New Code	Descriptor
81X43	Genetic testing for severe inherited conditions (eg, cystic fibrosis, Ashkenazi Jewish 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, GBA, GBE1, HBB, HEXA, IKBKAP, MCOLN1, PAH)

Test Purpose:
To detect carrier status in diseases relevant to severe inherited disease.

Method:
Next generation sequencing

Crosswalk Recommendation: Genomic Sequencing Procedure 81X43

New Code	Short Descriptor	Public Comment	Rationale
81X43	Genetic testing for severe inherited conditions	81412 - Ashkenazi Jewish associated disorders (eg, 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 ($2,448,56)	The methodologies and amount of resources required are similar for these clinically- similar codes.

Background and Test Purpose and Methods: Reconsidered Procedures (81334 and 81326)

New Code	Descriptor
81334	RUNX1 (runt related transcription factor 1) (eg, acute myeloid leukemia, familial platelet disorder with associated myeloid malignancy), gene analysis, targeted sequence analysis (eg, exons 3-8).
81326	PMP22 (peripheral myelin protein 22) (eg, Charcot-Marie-Tooth, hereditary neuropathy with liability to pressure palsies) gene analysis; known familial variant.

Test Purpose:
81334: To detect somatic mutations in genes associated with the diagnosis or prognosis of certain hematologic malignancies.
81326: To detect known familial variants in a patient suspected of being affected by autosomal dominant Charcot-Marie-Tooth or a related neuropathy.

Methods:
81334: PCR amplification followed by a genotyping method (i.e., sanger sequencing)
81326: For point mutations, PCR amplification and genotyping analysis is used. For del/dup analysis, a multiplex ligation dependent probe amplification (MLPA) is used.

Crosswalk Recommendations: Reconsidered Procedures (81334 and 81326)

Code	Gene Name	Public Comment	Rationale
81334	RUNX1	81259 - HBA1/HBA2 (alpha globin 1 and alpha globin 2) (eg, alpha thalassemia, Hb Bart hydrops fetalis syndrome, HbH disease), gene analysis; full gene sequence ($600.00)	The test methods used for sequencing analysis and the amount of DNA sequenced are comparable to that for 81259.
81326	PMP22	81215 - BRCA1 (breast cancer 1) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant ($375.25)	Similar methodologies and resources are used to detect known variants in BRCA which can be both point mutations or del/dups. Both conditions are autosomal dominant.