AMP Comments and Crosswalk Recommendations

2015 Clinical Lab Fee Schedule Public Meeting

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AMP Association for Molecular Pathology

Association for Molecular Pathology

- Professional scientific society (not-for-profit) that advances the clinical practice, science, and excellence of molecular and genomic laboratory medicine through education, innovation, and advocacy to enable highest quality health care.
- AMP represents more than 2,300 physicians, scientists, technologists and students who perform molecular diagnostic procedures

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Overview

- AMP submits these recommendations to help CMS develop the CY 2016 CLFS.
- Rationale and recommendations for the
  - 2016 CLFS Molecular Pathology Procedures
  - 2015 Molecular Pathology and Genomic Sequencing Procedures Reconsiderations
  - 2016 Genomic Sequencing Procedures

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2016 CLFS Molecular Pathology Procedures

CPT	Descriptor	Test Purpose and Method	Crosswalk Recommendation
81275 81276	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g., carcinoma) gene analysis; variants in codons 12 and 13 ; additional variant(s) (e.g., codon 61, codon 146)	KRAS codon 61 and codon 146 variants which are important to identify in patients with colorectal cancer as the presence of these mutations is a contraindication for use of targeted anti-EGFR monoclonal antibody therapy. Methods are typically PCR based.	81275. *KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g., carcinoma) gene analysis; variants in codons 12 and 13.* This code has similar resource utilization, has the same number of variants and is in the same gene code family as 81275.
812XX	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (e.g., acute myeloid leukemia), gene analysis, full gene sequence	This testing is for somatic mutations in AML. Typically performed by sequencing and requires 4 amplicons to cover the entire gene due to the larger size of this one exon.	81235. *EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis; common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q).* This code has similar resource utilization as 81235.
812XX	ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (e.g., acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain	For somatic mutations in CML which confer resistance to kinase inhibitors. It is done by sequencing and requires 6 amplicons to sequence the 6 exons of the gene that confer inhibitor resistance.	81235. *EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis; common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q).* This code has similar resource utilization as 81235.

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2016 CLFS Molecular Pathology Procedures

CPT	Descriptor	Test Purpose and Method	Crosswalk Recommendation
812XX	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)	NRAS activating mutations are important to identify in patients with colorectal cancer as the presence of these mutations is a contraindication for use of targeted anti-EGFR monoclonal antibody therapy. Methods are typically PCR based.	81275 times 1.5. *KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g., carcinoma) gene analysis; variants in codons 12 and 13.* This code has 1.5 times more resource utilization as 81275.
812XX	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis; targeted sequence analysis (e.g., exons 8, 11, 13, 17, 18)	This testing is for somatic mutations in a number of different tumors. It is done by sequencing and requires 5 amplicons to sequence.	81235. *EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis; common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q).* This code has similar resource utilization as 81235.
813XX	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (e.g., gastrointestinal stromal tumor [GIST]), gene analysis; targeted sequence analysis (e.g., exons 12, 18)	This testing is for somatic mutations in GIST (gastrointestinal stromal tumor) among other tumors which may confer resistance or sensitivity to kinase inhibitor therapy. It is done by sequencing and requires 5 amplicons to sequence.	81235. *EGFR (epidermal growth factor receptor) (e.g., non-small cell lung cancer) gene analysis; common variants (e.g., exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q).* This code has similar resource utilization as 81235.

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2016 CLFS Molecular Pathology Procedures

CPT	Descriptor	Test Purpose and Method	Crosswalk Recommendation
812XX	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (e.g., mastocytosis), gene analysis, D816 variant(s)	This testing is for somatic mutations in mastocytosis among other tumors and confers resistance to kinase inhibitor therapy. Methods are typically PCR based similar to BRAF V600E testing.	81210. *BRAF (v-raf murine sarcoma viral oncogene homolog B1) (e.g., colon cancer), gene analysis, V600E variant* This code has similar resource utilization as 81210.
812X20	CALR (calreticulin) (e.g., myeloproliferative disorders), gene analysis, common variants in exon 9	This testing is for somatic mutations in myeloproliferative neoplasms to confirm diagnosis and determine prognosis. Methods are typically PCR based similar to FLT3 ITD mutation testing.	81245. *FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis, internal tandem duplication (ITD) variants (i.e., exons 14, 15)* This code has similar resource utilization as 81245.
81211 812xx	BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb) ; full sequence analysis and full duplication/deletion analysis	This testing is for hereditary mutations in breast, ovarian and prostate cancers. Methods are typically a combination of sequencing and dup/del testing.	81211 PLUS 81213. *BRCA1, BRCA2 (breast cancer 1 and 2) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and common duplication/deletion variants in BRCA1 (i.e., exon 13 del 3.835kb, exon 13 dup 6kb, exon 14-20 del 26kb, exon 22 del 510bp, exon 8-9 del 7.1kb)* *BRCA1, BRCA2; uncommon duplication/deletion variants* This code has similar resource utilization as 81211 plus 81213.

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2015 Reconsideration Request

- For the four molecular pathology codes discussed last year, AMP is recommending crosswalks.
- These crosswalks were chosen because they require similar levels of resource utilization and either the same number of variants or similar RNA expression analysis.
- Note: Crosswalk valuation was used last year to price code G0464 Colorectal cancer screening; stool-based DNA and fecal occult hemoglobin (using a combination of 81315 PLUS 81275 PLUS 82274).

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2015 Molecular Pathology Codes

Code	CPT Descriptor	Test Purpose and Method	Crosswalk Recommendation
81246	FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (e.g., D835, I836)	For patients with AML, test is used to predict prognosis and treatment. Typically PCR based fragment analysis.	81245. *FLT3 (fms-related tyrosine kinase 3) (e.g., acute myeloid leukemia), gene analysis, internal tandem duplication (ITD) variants (i.e., exons 14, 15)* This code has similar resource utilization, has the same number of variants and is in the same gene code family as 81245.
81313	PCA3/KLK3 (prostate cancer antigen 3 [non-protein coding]/kallikrein-related peptidase 3 [prostate specific antigen]) ratio (e.g., prostate cancer)	Marker for prostate cancer. Quantitative reverse transcription PCR	81315. *PML/RARalpha, (t(15;17)), (PML-RARA regulated adaptor molecule 1) (e.g., promyelocytic leukemia) translocation analysis; common breakpoints (e.g., intron 3 and intron 6), qualitative or quantitative* This code uses identical types of resources with quantitative RNA expression analysis represented as a ratio of the target gene to a control as with 81315.

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2015 Molecular Pathology Codes

Code	CPT Descriptor	Test Purpose and Method	Crosswalk Recommendation
81288	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis	For patients with colorectal cancer with microsatellite instability; is used to determine whether they have sporadic CRC or hereditary Lynch syndrome which have different treatments and prognosis. Bisulfite DNA processing and DNA amplification.	81294. *MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants* This code has similar resource utilization, has the same number of variants and is in the same gene code family as 81294
81287	MGMT (O-6-methylguanine-DNA methyltransferase) (e.g., glioblastoma multiforme), methylation analysis	For patients with brain cancer; critical for therapy determination. Bisulfite DNA processing and DNA amplification.	81294. *MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants* This code has similar resource utilization as 81294.

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Genomic Sequencing Procedures (GSP) Recommendations Overview

- Show cost data collected by AMP to demonstrate actual costs
- Provide crosswalk recommendations for last year's and this year's GSP codes

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Genomic Sequencing Procedures

- Cost analyses of assays performed in representative laboratories was done for codes 81415 (3 laboratories), 81430 (2 laboratories) and 81445 (5 laboratories). The method used was similar to the process for determining the practice expense for the Physician Fee Schedule.

81415	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis
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
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, 5-50 genes (e.g., ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed

Micro-Cost to Identify All Components of Assay Cost

Cost Components	Description
Cost of Consumables/Supplies	Pricing for consumables and supplies
Equipment	Use of equipment associated with protocol Usually depreciated or attributed on a per test basis
Bioinformatics/Reporting	Software (commercial or internally developed), equipment, and time used to assess data generated by GSP
Personnel Time	Hands on time by laboratory personnel and those involved in reporting results (analysts, laboratory directors)
Validation, Maintenance, Overhead	Time and cost associated with preparing and keeping the assay ready for clinical use

These procedures require developing costing for development and use of bioinformatic pipeline, curation and reporting of results by higher skilled labor, and data storage

81445: Targeted genomic sequence analysis, solid organ neoplasm, 5-50 genes

	Laboratory	1	2	3	4	5
Sample Type/DNA Extraction Method		Tumor (Automated)	Blood (Manual)	Tumor (Manual)	Tumor (Manual)	Tumor (Automated)
Library Preparation Method		Ion AmpliSeq	Ion Ampliseq	Ion Ampliseq	Trusight Tumor	Trusight Tumor
Sequencing Platform		Ion Torrent	Ion Torrent	Ion Torrent	Illumina MiSeq	Illumina MiSeq
Bioinformatics/Data Analysis/Report Creation		Laboratory Director Review Custom Pipeline	Laboratory Director Review Custom Pipeline	Laboratory Director Review Custom Pipeline	Laboratory Director Review Custom Pipeline	Laboratory Director Review Commercial Pipeline
Total Labor Time	**DNA Extraction**	12	18.8	55	26	11
	Library Prep	31	26.62	44	34	25
	Sequencing	13	68	13	34	5
	Data Analysis	13	22	8	26	38
	Report Development	45	60	20	30	15
	Review/Sign-Out	9	8	8	10	15
Total Pre-Analytics/Analytics Consumables Cost	**DNA Extraction**	$ 6.28	$ 12.25	$ 10.21	$ 7.92	$ 5.47
	Library Prep	$ 207.68	$ 216.64	$ 181.87	$ 159.14	$ 163.08
	Sequencing	$ 85.30	$ 91.62	$ 75.56	$ 137.24	$ 180.25
Total Pre-Analytics/Analytics Equipment Cost	**DNA Extraction**	$ 0.15	$ 0.05	$ 0.23	$ 0.00	$ 0.09
	Library Prep	$ 3.12	$ 1.67	$ 10.22	$ 1.34	$ 7.56
	Sequencing	$ 6.21	$ 8.11	$ 6.89	$ 17.99	$ 21.46
Total Pre-Analytics/Analytics Labor Cost	**DNA Extraction**	$ 3.60	$ 5.64	$ 13.33	$ 13.71	$ 3.38
	Library Prep	$ 9.43	$ 7.99	$ 23.20	$ 18.29	$ 6.94
	Sequencing	$ 3.95	$ 20.34	$ 6.76	$ 18.29	$ 2.14
Total Bioinformatics / Data Analysis /Reporting Cost		$ 85.50	$ 243.49	$ 66.38	$ 110.00	$ 131.30
Total Validation Maintenance Overhead Cost		$ 287.34	$ 300.02	$ 194.77	$ 197.66	$ 56.31
Total Assay Cost (Per Sample)		$ 698.57	$ 907.82	$ 589.43	$ 681.58	$ 577.99

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5-50 gene Tumor Panel Cost Findings

- Cost range for 81445: $578 - $908
    - Cost variations due to library preparation and sequencing differences, investment in lab-developed or commercial bioinformatics and validation expenses
- Assays mostly based on commercial hotspot mutation panels from Ion Torrent or Illumina
  - Methods do not typically include duplication, deletions, CNV or translocation testing
  - Paired normal tissue testing for germ-line mutation determination was sometimes performed; we did not include those costs

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81430: Hearing loss, must include sequencing of at least 60 genes

	Laboratory	A	B
Sample Type/DNA Extraction Method		**Blood (Automated)**	**Blood (Manual)**
Library Preparation Method		**Agilent SureSelect**	**Agilent SureSelect**
Sequencing Platform		**Illumina HiSeq**	**Illumina HiSeq**
Bioinformatics/Data Analysis/Report Creation		**Group Review Custom Pipeline**	**Laboratory Director Review Custom Pipeline**
Total Labor Time	**DNA Extraction**	4	12
	Library Prep	41	20
	Sequencing	6	3
	Data Analysis	276	175
	Report Development	90	120
	Review/Sign-Out	45	8
Total Pre-Analytics/Analytics Consumables Cost	**DNA Extraction**	$ 4.76	$ 7.66
	Library Prep	$ 157.92	$ 180.60
	Sequencing	$ 788.18	$ 984.82
Total Pre-Analytics/Analytics Equipment Cost	**DNA Extraction**	$ 0.96	$ 0.03
	Library Prep	$ 3.26	$ 8.85
	Sequencing	$ 101.84	$ 93.89
Total Pre-Analytics/Analytics Labor Cost	**DNA Extraction**	$ 1.05	$ 3.53
	Library Prep	$ 12.15	$ 0.12
	Sequencing	$ 1.80	$ 0.75
Total Bioinformatics / Data Analysis /Reporting Cost		$ 670.88	$ 255.75
Total Validation Maintenance Overhead Cost		$ 206.67	$ 354.29
Total Assay Cost (Per Sample)		$ 1,949.47	$ 1,890.27

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Hearing Loss Panel Findings

- Costs range: $1890 - $1949
- Panels had almost exact same set of genes
- Largest variance in cost at technical sequencing and bioinformatic analysis components
- Duplication and/or deletions are typically assessed via another technology (microarray, PCR, FISH) and therefore were not included in micro-costing

81415: Exome

		Laboratory	I	II	III
Sample Type/DNA Extraction Method			Blood (Automated)	Blood (Manual)	Blood (Manual)
Library Preparation Method			Agilent SureSelect	Agilent SureSelect	Agilent SureSelect
Sequencing Platform			Illumina HiSeq	Illumina HiSeq	Illumina NextSeq
Bioinformatics/Data Analysis/Report Creation			Laboratory Director Review Custom Pipeline	Group Review Custom Pipeline	Group Review Custom Pipeline
Total Labor Time	**DNA Extraction**		0	12	24
	Library Prep		128	72	149
	Sequencing		18	5	6
	Data Analysis		45	10	95
	Report Development		12	840	204
	Review/Sign-Out		4	13	25
Total Pre-Analytics/Analytics Consumables Cost	**DNA Extraction**		$ 3.30	$ 7.66	$ 2.80
	Library Prep		$ 420.22	$ 276.25	$ 431.78
	Sequencing		$ 314.90	$ 988.70	$ 806.20
Total Pre-Analytics/Analytics Equipment Cost	**DNA Extraction**		$ 3.30	$ 0.03	$ 10.00
	Library Prep		$ 1.33	$ 17.10	$ 2.41
	Sequencing		$ 135.53	$ 103.73	$ 64.10
Total Pre-Analytics/Analytics Labor Cost	**DNA Extraction**		$ 3.30	$ 3.53	$ 7.20
	Library Prep		$ 38.40	$ 21.60	$ 44.70
	Sequencing		$ 5.40	$ -	$ 1.80
Total Bioinformatics / Data Analysis /Reporting Cost			$ 61.71	$ 1,669.59	$ 659.10
Total Validation Maintenance Overhead Cost			$ 410.21	$ 300.00	$ 398.36
Total Assay Cost (Per Sample)			$ 1,397.60	$ 3,388.18	$ 2,428.45

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Exome Findings

- Cost range: $1639 - $3142
- Focus was on the “medical” exome (variations with known significance)
- Considerable cost variability for technical sequencing and variant evaluation
  - Lowest cost assay had least data analysis expense due to a highly automated and efficient system of data analysis
  - Highest cost assay had more manual labor involved in the data analysis, interpretation and reporting

Genomic Sequencing Procedures

- Crosswalk based on relativity and similarity of resources to Tier 1 Molecular Pathology Procedures.
- 81292 for the *MLH1* gene is most commonly performed and has a representative number of exons (21) and coding sequence (2271 base pairs) for a gene.
- Comparison of traditional Sanger sequencing methods to that of equivalently sized genomic sequencing procedures demonstrate that genomic sequencing procedures are approximately one-fifth or 20% of the cost.
- Genomic sequencing procedures also require significant bioinformatic analysis which is not common for traditional Sanger sequencing and we recommend inclusion of 87901
  - HIV Infectious agent drug susceptibility phenotype prediction using regularly updated genotypic bioinformatics
- The method and resources of analyzing the nucleotide sequence to understand the alterations and predict the impact they may have overlaps very closely with the activity and resources involved in the bioinformatic analysis for genomic sequencing procedures and is relative to the amount of data being generated in the particular procedure.
- 87901 consists of the analysis of two HIV genes or approximate 1620 nucleotides similar to the amount of coverage in 81292.

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Genomic Sequencing Procedures - Continued

For example (below), the minimum required genes for 81410 is 9 and totals 240 exons. 20% of 240 is 48 exons. This is approximately 2 times the number of exons for the *MLH1* gene in code 81292. Given this relationship which includes the cost savings of performing genomic sequencing, we recommend a crosswalk of 81410 to 81292 and 87901 both times 2.

Code	CPT Descriptor	Rationale	Recommendation
81410	Aortic dysfunction or dilation (e.g., Marfan syndrome, Loeys Dietz syndrome, Ehler Danlos syndrome type IV, arterial tortuosity syndrome); genomic sequence analysis panel, must include sequencing of at least 9 genes, including FBN1, TGFBR1, TGFBR2, COL3A1, MYH11, ACTA2, SLC2A10, SMAD3, and MYLK	Minimum of 9 genes (240 exons). 240 times 20% = 48 48 divided by 21 = 2.28	Crosswalk to 81292 x 2 plus 87901 x 2

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Recommendation for Hearing Loss Genomic Sequence Analysis (81430)

- We could continue to use this math of calculating the minimum required exons per genomic sequencing procedure and apply a 20% reduction to determine the crosswalk. Interestingly, we identified that a simple mathematical relationship could be derived, in essence the natural log of the number of minimum genes, to determine the multiplier. In the above example the natural log (ln) of 9 genes is 2.198. We recommended the multiplier of 2. Furthermore, we do not believe that resources for genomic sequencing procedures with greater numbers of gene targets do not increase linearly which the application of the natural logarithm takes into account. We recommend scaling the resource increases with increasing numbers of genes using a natural logarithm scale to determine the multiply to apply to 81292.
- For code 81430, a minimum of 60 genes is requires. The natural log of 60 is 4.09. We recommend a crosswalk of 81292 and 87901 times 4.

Code	CPT Descriptor	Rationale	Recommendation
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	Min of 60 genes In(60) = 4	Crosswalk to 81292 x 4 plus 87901 x 4

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Recommendation for Exome Sequence Analysis (81415)

- Following this relationship For code 81415, approximately 20,000 genes are evaluated in performing exome analysis. The natural log of 20,000 is 9.9. We recommend a crosswalk of 81292 and 87901 times 9.9.

Code	CPT Descriptor	Rationale	Crosswalk Recommendation
81415	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis	~20,000 genes ln(20,000) = 9.9	Crosswalk to 81292 x 9.9 plus 87901 x 9.9

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Recommendations for Genomic Sequence Analysis Procedures: 81435, 81440, 81460, 81470

Code	CPT Descriptor	Rationale	Recommendation
81435	Hereditary colon cancer syndromes (e.g., Lynch syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include analysis of at least 7 genes, including APC, CHEK2, MLH1, MSH2, MSH6, MUTYH, and PMS2	Min of 7 genes ln(60) = 4	Crosswalk to 81292 x 2 plus 87901 x 2
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	Min of 100 genes ln2(100) = 4.6	Crosswalk to 81292 x 4.6 plus 87901 x 4.6
81460	Whole mitochondrial genome (e.g., 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	Min of 37 genes ln(37) = 3.6	Crosswalk to 81292 x 3.6 87901 x 3.6
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	Min of 60 genes ln(60) = 4	Crosswalk to 81292 x 4 87901 x 4

Recommendations for Targeted Genomic Sequence Analysis (81445, 81450, 81455)

Code	CPT Descriptor	Rationale	Recommendation
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, 5-50 genes (e.g., ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed	Median number of genes is (27) ln(27) = 3.29	Crosswalk with multiplier 81292 x 3 87901 x 3
81450	Targeted genomic sequence analysis panel, hematolymphoid neoplasm or disorder, DNA and RNA analysis when performed, 5-50 genes (e.g., BRAF, CEBPA, DNMT3A, EZH2, FLT3, IDH1, IDH2, JAK2, KRAS, KIT, MLL, NRAS, NPM1, NOTCH1), interrogation for sequence variants, and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed	Median number of genes is (27) ln(27) = 3.29	Crosswalk with multiplier 81292 x 3 87901 x 3
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA and RNA analysis when performed, 51 or greater genes (e.g., ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed	Most laboratory GSPs include 100 genes ln(100) = 4.6	Crosswalk to 81292 x 4.6 plus 87901 x 4.6

GSPs – Duplication/Deletion Analysis

These tests are performed in conjunction with the sequencing data from the base code in each family. We recommend using the CPT code 81294 with a multiplier based on a logarithm scale to determine each of the matched GSP sequencing codes.

GSPs – Duplication/Deletion Analysis

Code	CPT Descriptor	Crosswalk or Gapfill Recommendation
81411	Duplication/deletion analysis, panel must include analyses for TGFBR1, TGFBR2, MYH11, and COL3A1	Crosswalk with a multiplier 81294 x 1.4 Min of 4 genes ln(4) = 1.4
81431	Duplication/deletion analysis panel, must include copy number analyses for STRC and DFNB1 deletions in GJB2 and GJB6 genes	Crosswalk with a multiplier 81294 x 0.7 Min of 2 genes ln(2) = 0.7
81436	Duplication/deletion gene analysis panel, must include analysis of at least 8 genes, including APC, MLH1, MSH2, MSH6, PMS2, EPCAM, CHEK2, and MUTYH	Crosswalk with a multiplier 81294 x 2 Min of 7 genes Ln(8) = 2
81465	Whole mitochondrial genome large deletion analysis panel (e.g., Kearns-Sayre syndrome, chronic progressive external ophthalmoplegia), including heteroplasmy detection, if performed	Crosswalk with a multiplier 81294 x 3.6 Min of 37 genes ln(37) = 3.6
81471	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	Crosswalk with a multiplier 81294 x 4 Min of 60 genes ln(60) =4

Rationale for Recommendations for Other Genomic Sequencing Procedures

- The resources required for performing other genomic sequencing procedures was estimated based on the genetic content being evaluated.
- Recommendations are based on this similarity of resource utilization.

Recommendations for 2016 Genomic Sequencing Procedures: 814XB, 814XL, 814XM, 814XP

Code	CPT Descriptor	Rationale	Crosswalk Recommendation
814XB	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	Min of 9 genes ln(9) = 2.2	Crosswalk to 81292 x 2.2 plus 87901 x 2.2
814XL	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 14 genes, including ATM, BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11, and TP53	Min of 14 genes ln(14) = 2.6	Crosswalk to 81292 x 2.6 plus 87901 x 2.6
814XM	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	Min of 5 genes ln(5) = 1.6	Crosswalk to 81292 x 1.6 plus 87901 x 1.6
814XP	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	Min of 15 genes ln(15) = 2.7	Crosswalk to 81292 x 2.7 plus 87901 x 2.7

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Recommendations for 2016 Genomic Sequencing Procedures: 814XE, 814XF, 814XD

Code	CPT Descriptor	Rationale	Crosswalk Recommendation
814XE	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	Min of 6 genes ln(6) = 1.8	Crosswalk to 81292 x 1.8 plus 87901 x 1.8
814XF	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	Min of 4 genes ln(4) = 1.4	Crosswalk to 81292 x 1.4 plus 87901 x 1.4
814XD	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	Min of 12 genes ln(12) = 2.5	Crosswalk to 81292 x 2.5 plus 87901 x 2.5

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2016 GSPs – Duplication/Deletion Analysis

Code	CPT Descriptor	Crosswalk or Gapfill Recommendation
814x06	duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL	Crosswalk with a multiplier 81294 x 1.4 Min of 4 genes ln(4) = 1.4
814x13	duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11	Crosswalk with a multiplier 81294 x 1.6 Min of 5 genes ln(5) = 1.6

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Thank You

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