1. Variantyx, Inc.

Presenters: Daryl Spinner and Christine Stanley

Codes: 0212U, 0213U, 0214U, 0215U, 0216U, 0217U, 0218U

CMS CLFS Annual Public Meeting | 22 June 2020

Transforming genomic diagnostics and personalized medicine

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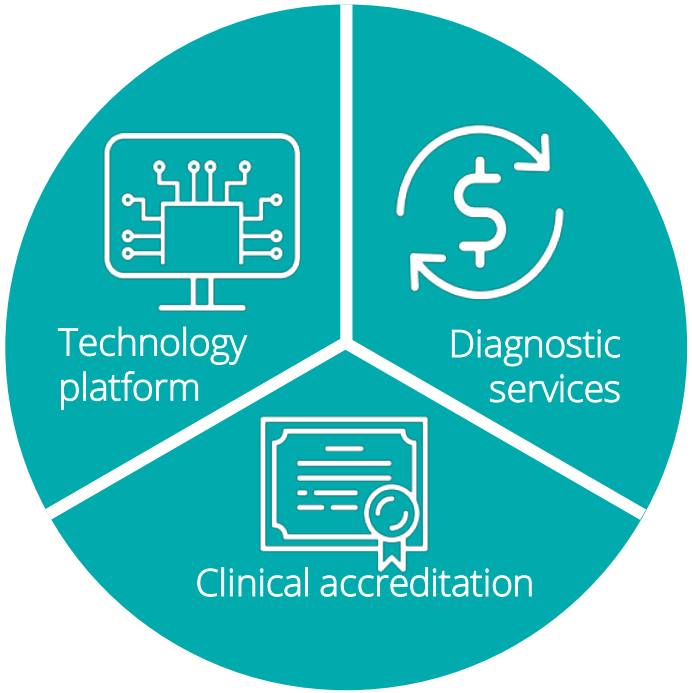
Variantyx PLA Codes Under CLFS Consideration

Item #	Code #	Proprietary Laboratory Analyses Test	Proposed Fee Setting Approach
109	0212U	Genomic Unity® Whole Genome Analysis – Proband	Crosswalk ≈ $11,896.24
110	0213U	Genomic Unity® Whole Genome Analysis – Comparator	Crosswalk ≈ $9,574.99
111	0214U	Genomic Unity® Exome Plus Analysis – Proband	Crosswalk ≈ $11,645.04
112	0215U	Genomic Unity® Exome Plus Analysis – Comparator	Crosswalk ≈ $18,865.04
113	0216U	Genomic Unity® Ataxia Repeat Expansion and Sequence Analysis	Crosswalk ≈ $2,813.80
114	0217U	Genomic Unity® Comprehensive Ataxia Repeat Expansion and Sequence Analysis	Crosswalk ≈ $3,197.80
115	0218U	Genomic Unity® DMD Analysis	Crosswalk ≈ $2,584.90

Who Is Variantyx?

- Founded in 2014 and headquartered in Boston Massachusetts, Variantyx is a CLIA/CAP accredited diagnostic lab and a leading provider of advanced genomic diagnostic solutions to clinicians and labs.
- **Variantyx Genomic Intelligence® is the industry's first clinically accredited comprehensive WGS-based analytical platform**. Built using proprietary state-of-the-art algorithms, the platform is clinically validated with hundreds of samples.
- **Genomic Unity® is the industry's first comprehensive WGS-based diagnostic test, combining all genomic tests into one to provide: Improved diagnostic yield, shorter diagnostic odyssey and lower cost to payors**.
- Variantyx products have been adopted by world-leading clinical institutions and reimbursed under existing CPT codes by the major US health insurance payors.
- Variantyx is experiencing rapid growth in tests accessioned due to provider and payor recognition of the **advantages of genomic testing on a WGS-based platform for testing ranging from single gene to whole exome**.



WGS = whole genome sequence

Background On Disease-Causing Genomic Variants

Multiple types of genomic variants cause genetic disorders and inherited cancers

Genomic Variant Types/ DNA Changes	Details	Example Indications
Small sequence changes	Single nucleotide variants (SNVs), insertions or deletions [indels] of less than 35 bp	Hereditary breast and ovarian cancers; inherited cardiovascular and neurodevelopmental disorders
Deletions and/or duplications and copy number variations (CNVs)	Ranging from 35 bp up to whole chromosomes	Duchenne muscular dystrophy; spinal muscular atrophy; hereditary connective tissue disorders
Inversions	Regions of DNA that are inverted from their normal orientation	Hemophilia
Short tandem repeat (STR) expansions	Short repetitive sequences in genes that expand in number of repeats	Multiple forms of ataxia, movement disorders and intellectual disability
Mitochondrial genome variants	Sequence changes and deletions/ duplications of any size	Severe inherited neurological and metabolic disorders
Aneuploidy/ mosaic aneuploidy	Duplications of entire chromosomes that may only be present in some cells	Chromosomal disorders marked by dysmorphic features
Loss of heterozygosity (LOH)/ uniparental disomy (UPD)	Changes in the DNA arising from abnormalities in how chromosomes were inherited from mother and father	Multiple forms of severe intellectual disability
Transposable element insertions/ mobile element insertions	Abnormal pieces of DNA that insert and move around the genome causing heritable disease	Forms of inherited muscular dystrophy

Background On Relevant Comparator Tests On CLFS

Relevant Tier 1 and Tier 2 MoPath tests on the CLFS *DO NOT* anticipate detection of all genomic variant types

Currently Available CLFS-Listed Genomic Tests (CPTs)	Detection *INCLUDED* in CLFS Payment	Detection *NOT INCLUDED* in CLFS Payment
Whole genome (81425, 81426)	Small sequence variants in nuclear genes and known intronic and intergenic variants	Deletion/ duplications, CNVs, STR expansions, mitochondrial genome variants, multiple variant types in combination
Whole exome (81415, 81416)	Small sequence variants in nuclear genes	Deletion/ duplications, CNVs, STR expansions, mitochondrial genome variants, multiple variant types in combination
Multi-gene panels (e.g., 81161 – 81164, 81410 – 81471)	Small sequence variants *AND/OR* deletions/ duplications	STR expansions, CNVs, multiple variant types in combination
Single-gene analyses (e.g., 81165 – 81227, 81243, 81404 – 81408)	Small sequence variants *OR* deletions/ duplications *OR* STR expansions	STR expansions, CNVs, multiple variant types in combination

CNVs = copy number variants, STR = short tandem repeat

Proposed PLA Code Fee Schedule Approach

Crosswalk most relevant given direct comparability to tests with existing CPT codes

PLA Test	Equivalent Comparator
0212U: Genomic Unity® Whole Genome Analysis – Proband	1. Genome + 2. Cytogenomic *high resolution* constitutional (genome-wide) interrogation of genomic regions for CNVs + 3. 26-gene short tandem repeat expansion analyses + 4. Whole mitochondrial genome sequence + 5. Whole mitochondrial genome large deletion analysis panel
0213U: Genomic Unity® Whole Genome Analysis – Comparator	1. Genome, each comparator + 2. Cytogenomic *high resolution* constitutional (genome-wide) interrogation of genomic regions for CNVs + 3. 26-gene short tandem repeat expansion analyses + 4. Whole mitochondrial genome sequence + 5. Whole mitochondrial genome large deletion analysis panel
0214U: Genomic Unity® Exome Plus Analysis – Proband	1. Exome + 2. Cytogenomic *high resolution* constitutional (genome-wide) interrogation of genomic regions for CNVs + 3. 26-gene short tandem repeat expansion analyses + 4. Whole mitochondrial genome sequence + 5. Whole mitochondrial genome large deletion analysis panel
0215U: Genomic Unity® Exome Plus Analysis – Comparator	1. Exome, each comparator + 2. Cytogenomic *high resolution* constitutional (genome-wide) interrogation of genomic regions for CNVs + 3. 26-gene short tandem repeat expansion analyses + 4. Whole mitochondrial genome sequence + 5. Whole mitochondrial genome large deletion analysis panel

CNVs = copy number variants, DMD = Duchenne and Becker muscular dystrophy (dystrophin) gene

Proposed PLA Code Fee Schedule Approach *(cont'd)*

Crosswalk most relevant given direct comparability to tests with existing CPT codes

PLA Test	Equivalent Comparator
0216U: Genomic Unity® Ataxia Repeat Expansion and Sequence Analysis	1. 12 single gene short tandem repeat expansion tests + 2. 12-gene full gene sequence panel + 3. 12-gene deletion/ duplication panel
0217U: Genomic Unity® Comprehensive Ataxia Repeat Expansion and Sequence Analysis	1. 12 single gene short tandem repeat expansion tests + 2. 51-gene full gene sequence panel + 3. 51-gene deletion/ duplication panel
0218U: Genomic Unity® DMD Analysis	1. DMD full gene sequence analysis + 2. DMD deletion/ duplication analysis

CNVs = copy number variants, DMD = Duchenne and Becker muscular dystrophy (dystrophin) gene

0212U: Genomic Unity® Whole Genome Analysis – Proband

Public Comment	Rationale
• 81425: ($5,031.20) • 81229: ($1,160.00) • 81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81343, 81344: ($137.00 TIMES 17 = $2,329.00) • 81243: ($57.04) • 81479: ($137.00 TIMES 8 = $1,096.00) • 81460: ($1,287.00) • 81465: ($936.00) **TOTAL = $11,896.24**	Level of service equivalent to totality of code descriptors

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0212U: Genomic Unity® Whole Genome Analysis – Proband

Genomic Unity® Whole Genome Analysis – Proband

Whole genome
+
High-resolution constitutional genome-wide copy number analysis
+
Multi-gene STR expansion analysis
+
Comprehensive mitochondrial genome analysis

	CPT	2020 CLFS
Standard genome	81425	$5,031.20
+		
CMA* constitutional genome-wide CNV analysis *(CMA resolution limited to ≥20 kb - 400 kb)*	81229	$1,160.00
+		
26-gene tandem repeat expansion analyses *(AFF2, AFF3, AR, ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, ATXN10, C9ORF72, CACNA1A, CNBP, CSTB, DIP2B, DMPK, FMR1, FXN, HTT, JPH3, NOP56, NOTCH2NLC, PHOX2B, PPP2R2B, TBP, TCF4)*	81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81323, 81344 81243 81479 x 8	17 x $137.00 = $2,329.00 1 x $ 57.04 = $ 57.04 8 x $137.00 = $1,096.00 $3,482.04
+		
Mitochondrial whole genome sequence	81460	$1,287.00
+		
Mitochondrial whole genome deletion/ duplication analysis	81465	$ 936.00
0212U		**>$11,896.24**

Most Relevant Comparator Equivalents

* CMA = chromosomal microarray analysis, CNV = copy number variant, STR = short tandem repeat

0213U: Genomic Unity® Whole Genome Analysis – Comparator

Public Comment	Rationale
• 81426: ($2,709.95) • 81229: ($1,160.00) • 81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81343, 81344: ($137.00 TIMES 17 = $2,329.00) • 81243: ($57.04) • 81479: ($137.00 TIMES 8 = $1,096.00) • 81460: ($1,287.00) • 81465: ($936.00) **TOTAL = $9,574.99**	Level of service equivalent to totality of code descriptors

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0213U: Genomic Unity® Whole Genome Analysis – Comparator

Genomic Unity® Whole Genome Analysis – Comparator

Whole genome comparator
+
High-resolution constitutional genome-wide copy number analysis
+
Multi-gene STR expansion analysis
+
Comprehensive mitochondrial genome analysis

	CPT	2020 CLFS
Standard genome comparator	81426	$2,709.95
+		
CMA* constitutional genome-wide CNV analysis *(CMA resolution limited to ≥20 kb - 400 kb)*	81229	$1,160.00
+		
26-gene tandem repeat expansion analyses *(AFF2, AFF3, AR, ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, ATXN10, C9ORF72, CACNA1A, CNBP, CSTB, DIP2B, DMPK, FMR1, FXN, HTT, JPH3, NOP56, NOTCH2NLC, PHOX2B, PPP2R2B, TBP, TCF4)*	81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81323, 81344 81243 81479 x 8	17 x $137.00 = $2,329.00 1 x $ 57.04 = $ 57.04 8 x $137.00 = $1,096.00 $3,482.04
+		
Mitochondrial whole genome sequence	81460	$1,287.00
+		
Mitochondrial whole genome deletion/ duplication analysis	81465	$ 936.00
0213U		**>$9,574.99**

Most Relevant Comparator Equivalents

* CMA = chromosomal microarray analysis, CNV = copy number variant, STR = short tandem repeat

0214U: Genomic Unity® Exome Plus Analysis – Proband

Public Comment	Rationale
• 81415: ($4,780.00) • 81229: ($1,160.00) • 81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81343, 81344: ($137.00 TIMES 17 = $2,329.00) • 81243: ($57.04) • 81479: ($137.00 TIMES 8 = $1,096.00) • 81460: ($1,287.00) • 81465: ($936.00) **TOTAL = $11,645.04**	Level of service equivalent to totality of code descriptors

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0214U: Genomic Unity® Exome Plus Analysis – Proband

Genomic Unity® Exome Plus Analysis – Proband

Whole exome
+
High-resolution constitutional genome-wide copy number analysis
+
Multi-gene STR expansion analysis
+
Comprehensive mitochondrial genome analysis

	CPT	2020 CLFS
Standard exome	81415	$4,780.00
+		
CMA* constitutional genome-wide CNV analysis *(CMA resolution limited to ≥20 kb - 400 kb)*	81229	$1,160.00
+		
26-gene tandem repeat expansion analyses *(AFF2, AFF3, AR, ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, ATXN10, C9ORF72, CACNA1A, CNBP, CSTB, DIP2B, DMPK, FMR1, FXN, HTT, JPH3, NOP56, NOTCH2NLC, PHOX2B, PPP2R2B, TBP, TCF4)*	81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81323, 81344 81243 81479 x 8	17 x $137.00 = $2,329.00 1 x $ 57.04 = $ 57.04 8 x $137.00 = $1,096.00 $3,482.04
+		
Mitochondrial whole genome sequence	81460	$1,287.00
+		
Mitochondrial whole genome deletion/ duplication analysis	81465	$ 936.00
	0214U	**>$11,645.04**

Most Relevant Comparator Equivalents

* CMA = chromosomal microarray analysis, CNV = copy number variant, STR = short tandem repeat

0215U: Genomic Unity® Exome Plus Analysis – Comparator

Public Comment	Rationale
• 81416: ($12,000) • 81229: ($1,160.00) • 81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81343, 81344: ($137.00 TIMES 17 = $2,329.00) • 81243: ($57.04) • 81479: ($137.00 TIMES 8 = $1,096.00) • 81460: ($1,287.00) • 81465: ($936.00) **TOTAL = $18,865.04**	Level of service equivalent to totality of code descriptors

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0215U: Genomic Unity® Exome Plus Analysis – Comparator

Genomic Unity® Exome Plus Analysis – Comparator

Whole exome comparator
+
High-resolution constitutional genome-wide copy number analysis
+
Multi-gene STR expansion analysis
+
Comprehensive mitochondrial genome analysis

	CPT	2020 CLFS
Standard exome comparator	81416	$12,000.00
+		
CMA* constitutional genome-wide CNV analysis *(CMA resolution limited to ≥20 kb - 400 kb)*	81229	$1,160.00
+		
26-gene tandem repeat expansion analyses *(AFF2, AFF3, AR, ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, ATXN10, C9ORF72, CACNA1A, CNBP, CSTB, DIP2B, DMPK, FMR1, FXN, HTT, JPH3, NOP56, NOTCH2NLC, PHOX2B, PPP2R2B, TBP, TCF4)*	81171, 81204, 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81187, 81188, 81234, 81284, 81271, 81323, 81344 81243 81479 x 8	17 x $137.00 = $2,329.00 1 x $ 57.04 = $ 57.04 8 x $137.00 = $1,096.00 $3,482.04
+		
Mitochondrial whole genome sequence	81460	$1,287.00
+		
Mitochondrial whole genome deletion/ duplication analysis	81465	$ 936.00
	0215U	**>$18,865.04**

Most Relevant Comparator Equivalents

* CMA = chromosomal microarray analysis, CNV = copy number variant, STR = short tandem repeat

0216U: Genomic Unity® Ataxia Repeat Expansion and Sequence Analysis

Public Comment	Rationale
• 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81284, 81343, 81344: ($137.00 TIMES 11 = $1,507.00) • 81479: ($137.00) • ≈ 81435: ($584.90) • ≈ 81436: ($584.90) • **TOTAL = $2,813.80**	Level of service equivalent to totality of code descriptors

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0216U: Genomic Unity® Ataxia Repeat Expansion and Sequence Analysis (12 gene)

Genomic Unity® Ataxia Repeat Expansion and Sequence Analysis

Multi-gene STR* expansion analysis
+
Multi-gene sequence panel
+
Multi-gene deletion/duplication panel

	CPT	2020 CLFS
12-gene short tandem repeat expansion analyses *(ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, ATXN10, CACNA1A, FXN, NOP56, PPP2R2B, TBP)*	81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81284, 81343, 81344, 81479	12 x $137.00 = $1,644.00
+		
12-gene sequencing panel (e.g., ≈ 10-gene hereditary colon cancer disorders sequence analysis panel)	≈ 81435	$584.90
+		
12-gene deletion/ duplication panel (e.g., ≈ 10-gene hereditary colon cancer disorders deletion/ duplication analysis panel)	≈ 81436	$584.90
		0216U ≈ $2,813.80

Most Relevant Comparator Equivalents

* STR = short tandem repeat

0217U: Genomic Unity® Comprehensive Ataxia Repeat Expansion and Sequence Analysis

Public Comment	Rationale
• 81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81284, 81343, 81344: ($137.00 TIMES 11 = $1,507.00) • 81479: ($137.00) • 81470: ($914.00 TIMES 51/60 = $776.90) • 81471: ($914.00 TIMES 51/60 = $776.90) • **TOTAL = $3,197.80**	Level of service equivalent to totality of code descriptors

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0217U: Genomic Unity® Comprehensive Ataxia Repeat Expansion and Sequence Analysis (51 genes)

Genomic Unity® Comprehensive Ataxia Repeat Expansion and Sequence Analysis

Multi-gene STR* expansion analysis
+
Multi-gene sequence panel
+
Multi-gene deletion/duplication panel

	CPT 2020 CLFS
12-gene short tandem repeat expansion analyses *(ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, ATXN10, CACNA1A, FXN, NOP56, PPP2R2B, TBP)*	81177, 81178, 81179, 81180, 81181, 81182, 81183, 81184, 81284, 81343, 81344, 81479 12 x $137.00 = $1,644.00
+	
51-gene sequencing panel (e.g., ≈ 60-gene X-linked intellectual disabilities sequence analysis panel)	≈ 81470 x 51/60 51/60 x $914.00 = $776.90
+	
51-gene deletion/duplication panel (e.g., ≈ 60-gene hereditary colon cancer disorders deletion/ duplication analysis panel)	≈ 81471 x 51/60 51/60 x $914.00 = $776.90
	0217U ≈ $3,197.80

Most Relevant Comparator Equivalents

* STR = short tandem repeat

0218U: Genomic Unity® DMD Analysis

Public Comment	Rationale
• 81408: ($2,000.00) • 81161: ($584.90) • **TOTAL = $2,584.90**	Level of service equivalent to totality of code descriptors

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0218U: Genomic Unity® DMD Analysis

Genomic Unity® DMD Analysis

DMD full gene sequence
+
DMD deletion/duplication analysis

	CPT	2020 CLFS
DMD full gene sequence analysis	81408	$2,000.00
+		
DMD deletion/ duplication analysis	81161	$584.90

0218U ≈ $2,584.90

Most Relevant Comparator Equivalents

Thank you