Centers for Medicare and Medicaid Services

Clinical Laboratory Fee Schedule Annual Laboratory Public Meeting

June 22, 2020

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Association for Molecular Pathology

Outline

- Reconsidered – Molecular Pathology
  - PALB2 Full Gene Sequence (81307)
- New – Molecular Pathology
  - CCND1/IGH translocation analysis (8X010)
  - IGH@/BCL2 translocation analysis (8X009)
  - JAK2 targeted sequence analysis (8X008)
  - MPL family (8X006, 8X007)
  - NTRK family (8X020, 8X000, 8X001, and 8X002)
  - SF3B1 common variants (8XX00)
  - SRSF2 common variants (8XX01)
  - TP53 family (8X003, 8X005, 8X004)
  - U2AF1 common variants (8XX02)
  - ZRSR2 common variant(s) (8XX03)
- New-Genomic Sequencing Procedures
  - Epilepsy genomic sequence analysis panel (81XX6)
- New-Multianalyte Assays with Algorithmic Analyses (MAAAs)
  - Infectious disease, bacterial vaginosis (81XX4)
  - Infectious disease, bacterial vaginosis and vaginitis (815X3)
- New – Microbiology
  - Infectious Agent Detection by Nucleic Acid; SARS-CoV-2 (87635)

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

Reconsidered – Molecular Pathology

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81307: PALB2 gene analysis; full gene sequence

Purpose: To detect variants in PALB2 in pre-cancer or cancer.

Method: High quality genomic DNA is isolated from whole blood, and is subjected to Sanger sequencing of the PALB2 gene.

Public Comment	Rationale
81317- PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis ($676.50)	The methodology, resources, and amount of genetic material sequenced are comparable to that of PMS2 (81317)

New – Molecular Pathology

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New Molecular Pathology Codes

- Translocation Analysis Codes:
  - CCND1/IGH translocation analysis (8X010)
  - IGH@/BCL2 translocation analysis (8X009)
- Targeted Sequence Analysis Codes:
  - JAK2 targeted sequence analysis (8X008)
- Common Variants Codes:
  - SF3B1 common variants (8XX00)
  - SRSF2 common variants (8XX01)
  - U2AF1 common variants (8XX02)
  - ZRSR2 common variant(s) (8XX03)
- Gene families:
  - MPL codes (8X006, 8X007)
  - NTRK codes (8X020, 8X000, 8X001, and 8X002)
  - TP53 codes (8X003, 8X005, 8X004)

Translocation Analysis Codes – CCND1/IGH and IGH@/BCL2 (8X010, 8X009)

- **Purpose:** To confirm diagnosis of specific types of lymphoma
- **Method:** High quality genomic DNA is isolated from whole blood, bone marrow, or formalin-fixed paraffin-embedded tissue, and is subjected to testing of the specific translocation by PCR amplification.

Code #	Long Code Descriptor
8X010	CCND1/IGH (t(11;14)) (eg, mantle cell lymphoma) translocation analysis, major breakpoint, qualitative and quantitative, if performed
8X009	IGH@/BCL2 (t(14;18)) (eg, follicular lymphoma) translocation analysis, major breakpoint region (MBR) and minor cluster region (mcr) breakpoints, qualitative or quantitative

Translocation Analysis Codes – CCND1/IGH and IGH@/BCL2 (8X010, 8X009)

Code #	Public Comment	Rationale
8X010	**81315** - PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative ($207.31)	The methodology, resources, and amount of genetic material sequenced are comparable to that of translocation analysis for PML-RARA
8X009	**81315** - PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative ($207.31)	The methodology, resources, and amount of genetic material sequenced are comparable to that of translocation analysis for PML-RARA

8X008 – JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) targeted sequence analysis (eg, exons 12 and 13)

Purpose: For diagnosis of polycythemia vera, when JAK2 V617F point mutation testing was negative.

Method: High quality genomic DNA is isolated from whole blood or bone marrow, and is subjected to targeted sequencing of JAK2 exons 12 and 13.

Public Comment	Rationale
81272- KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, gastrointestinal stromal tumor [GIST], acute myeloid leukemia, melanoma), gene analysis, targeted sequence analysis (eg, exons 8, 11, 13, 17, 18) ($329.51)	The methodology, resources, and amount of genetic material sequenced are comparable to that of KIT targeted sequence analysis

Common Variant Analysis Codes (8XX00, 8XX01, 8XX02, 8XX03)

- **Purpose:** To aid in the diagnosis of myelodysplastic syndrome or other myeloid neoplasms
- **Method:** High quality genomic DNA is isolated from whole blood or bone marrow, and is subjected to targeted sequencing of specific common variants of a gene.

Code #	Long Code Descriptor
8XX00	SF3B1 (splicing factor [3b] subunit B1) (eg, myelodysplastic syndrome/acute myeloid leukemia) gene analysis, common variants (eg, A672T, E622D, L833F, R625C, R625L)
8XX01	SRSF2 (serine and arginine-rich splicing factor 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, P95H, P95L)
8XX02	U2AF1 (U2 small nuclear RNA auxiliary factor 1) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variants (eg, S34F, S34Y, Q157R, Q157P)
8XX03	ZRSR2 (zinc finger CCCH-type, RNA binding motif and serine/arginine-rich 2) (eg, myelodysplastic syndrome, acute myeloid leukemia) gene analysis, common variant(s) (eg, E65fs, E122fs, R448fs)

Common Variant Analysis Codes (8XX00, 8XX01, 8XX02, 8XX03)

Code #	Public Comment	Ratinale
8XX00	**81120** - IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C) ($193.25)	The methodology, resources, and amount of genetic material sequenced are comparable to that of IDH1 common variants. Both assess genes for an oncology disorder and similar number of variants.
8XX01	**81233** - BTK (Bruton's tyrosine kinase) (eg, chronic lymphocytic leukemia) gene analysis, common variants (eg, C481S, C481R, C481F) ($175.40)	The methodology, resources, and amount of genetic material sequenced are comparable to that of BTK common variants. Both assess genes for an oncology disorder and similar number of variants.
8XX02	**81120** - IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C) ($193.25)	The methodology, resources, and amount of genetic material sequenced are comparable to that of IDH1 common variants. Both assess genes for an oncology disorder and similar number of variants.
8XX03	**81120** - IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C) ($193.25)	The methodology, resources, and amount of genetic material sequenced are comparable to that of IDH1 common variants. Both assess genes for an oncology disorder and similar number of variants.

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MPL Codes (8X006, 8X007)

- **Purpose:** For diagnosis of a myeloproliferative neoplasm.
- **Method:** High quality genomic DNA is isolated from whole blood or bone marrow, and is subjected to analysis of MPL gene

Code #	Long Code Descriptor
8X006	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; common variants (eg, W515A, W515K, W515L, W515R)
8X007	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; sequence analysis, exon 10

MPL Codes (8X006, 8X007)

- **Purpose:** For diagnosis of a myeloproliferative neoplasm.
- **Method:** High quality genomic DNA is isolated from whole blood or bone marrow, and is subjected to analysis of MPL gene

Code #	Public Comment	Rationale
8X006	**81120 -** IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C) ($193.25)	The methodology, resources, and amount of genetic material sequenced are comparable to that of IDH1 common variants (both are testing of variants in one codon in oncology samples)
8X007	**81310** - NPM1 (nucleophosmin) (eg, acute myeloid leukemia) gene analysis, exon 12 variants ($246.52)	The methodology, resources, and amount of genetic material sequenced are comparable to that of NPM1 gene analysis (both are 1 exon targeted sequencing for oncology samples)

NTRK Codes (8X020, 8X000, 8X001, 8X002)

- **Purpose:** To determine treatment options for solid tumors.
- **Method:** High quality nucleic acids are isolated from fresh or formalin fixed paraffin embedded tumor tissue and subjected to testing of genomic rearrangements by real-time PCR amplification.

Code #	Long Code Descriptor
8X020	NTRK (neurotrophic-tropomyosin receptor tyrosine kinase 1, 2, and 3) (eg, solid tumors) translocation analysis
8X000	NTRK1 (neurotrophic receptor tyrosine kinase 1) (eg, solid tumors) translocation analysis
8X001	NTRK2 (neurotrophic receptor tyrosine kinase 2) (eg, solid tumors) translocation analysis
8X002	NTRK3 (neurotrophic receptor tyrosine kinase 3) (eg, solid tumors) translocation analysis

NTRK Codes (8X020, 8X000, 8X001, 8X002)

Code #	Public Comment	Rationale
8X020	**81315 X 2.5 -** PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative ($207.31 X 2.5 = 518.26)	The methodology, resources, and amount of genetic material sequenced are comparable to that of 81315 X 2.5
8X000	**81315 -** PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative ($207.31)	The methodology, resources, and amount of genetic material sequenced are comparable to that of PML/RARalpha translocation analysis
8X001	**81315 -** PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative ($207.31)	The methodology, resources, and amount of genetic material sequenced are comparable to that of PML/RARalpha translocation analysis
8X002	**81315** -PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative ($207.31)	The methodology, resources, and amount of genetic material sequenced are comparable to that of PML/RARalpha translocation analysis

TP53 Codes (8X003, 8X005, 8X004)

- **Purpose:** to detect pathogenic or likely pathogenic variants (e.g., SNVs and small indels) in the TP53 gene.
- **Method:** High quality DNA is isolated from peripheral whole blood and is subjected to Sanger sequencing

Code #	Long Code Descriptor
8X003	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; full gene sequence
8X005	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; known familial variant
8X004	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (eg, 4 oncology)

TP53 Codes (8X003, 8X005, 8X004)

Code #	Public Comment	Rationale
8X003	**81298** - MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis ($641.85)	The methodology, resources, and amount of genetic material sequenced are comparable to that of MSH6 full sequence analysis. Both assess germline cancer disposition genes and are relatively the same size.
8X005	**81299** - MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants ($308.00)	The methodology, resources, and amount of genetic material sequenced are comparable to that of MSH6 known familial variants. Both assess known familial variants in germline cancer disposition genes
8X004	**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) ($329.51)	The methodology, resources, and amount of genetic material sequenced are comparable to that of RUNX1 known familial variants. Both assess targeted sequences in cancer-related genes.

New – Genomic Sequencing Procedures

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81XX6 – 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

Purpose: To detect pathogenic or likely pathogenic variants (single nucleotide and small insertion or deletion) in genes associated with epilepsy

Method: Massively parallel sequencing (next generation) sequencing of at least 24 genes

Public Comment	Rationale
81413 X 2 - Cardiac ion channelopathies (eg, Brugada syndrome, long QT syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia); genomic sequence analysis panel, must include sequencing of at least 10 genes, including ANK2, CASQ2, CAV3, KCNE1, KCNE2, KCNH2, KCNJ2, KCNQ1, RYR2, and SCN5A ($584.90 X 2 = $1,169.80)	All methods are genomic sequencing procedures for inherited conditions and use similar amounts of resources needed to perform testing

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New – Multianalyte Assays with Algorithmic Analyses (MAAAs)

81XX4 – Infectious disease, bacterial vaginosis, quantitative real-time amplification of RNA markers for Atopobium vaginae, Gardnerella vaginalis, and Lactobacillus species, utilizing vaginal fluid specimens, algorithm reported as a positive or negative result for bacterial vaginosis

Purpose: Detection and quantitation of ribosomal RNA from each of the bacteria associated with bacterial vaginosis (BV), including Lactobacillus (L. gasseri, L. crispatus, and L. jensenii), Gardnerella vaginalis, and Atopobium vaginae.

Method: an in vitro nucleic acid amplification test that utilizes real time transcription-mediated amplification (TMA)

Public Comment	Rationale
87631- Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets ($142.63)	The technology, workflow, and type and amount of analytes are similar in both 81XX4 and 87631

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815X3 – Infectious disease, bacterial vaginosis and vaginitis, quantitative real-time amplification of DNA markers for Gardnerella vaginalis, Atopobium vaginae, Megasphaera Type 1, Bacterial Vaginosis Associated Bacteria-2 (BVAB-2), and Lactobacillus species (L. crispatus and L. jensenii), utilizing vaginal fluid specimens, algorithm reported as a positive or negative for high likelihood of bacterial vaginosis, includes separate detection of Trichomonas vaginalis and/or Candida species (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata, Candida krusei, when reported

Purpose: Detection of bacterial vaginosis and vaginitis

Method: quantitative real-time amplification of DNA markers for Gardnerella vaginalis, Atopobium vaginae, Megasphaera Type 1, Bacterial Vaginosis Associated Bacteria-2 (BVAB-2), and Lactobacillus species (L. crispatus and L. jensenii) with the algorithm reported as a positive or negative for high likelihood of bacterial vaginosis. Also includes separate detection of Trichomonas vaginalis and/or Candida species (C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis), Candida glabrata, Candida krusei, when reported

Public Comment	Rationale
87506 -Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, Clostridium difficile, E. coli, Salmonella, Shigella, norovirus, Giardia), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 6-11 targets ($262.99)	Both 815X3 and 87506 require similar instrumentation, technology, and resource utilization

New - Microbiology

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87635: Infectious agent detection by nucleic acid (DNA or RNA); severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19]), amplified probe technique

Purpose: Purpose: to diagnose infection with SARS-CoV-2; to determine if virus is present or absent

Method: Method: multiplex reverse transcription PCR and mutliplex amplified probe technique

Public Comment	Rationale
U0003 - Infectious agent detection by nucleic acid (DNA or RNA); Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19]), amplified probe technique, making use of high throughput technologies as described by CMS-2020-01-R ($100) *Option 2 – 87502 - Infectious agent detection by nucleic acid (DNA or RNA); influenza virus, for multiple types or sub-types, includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, first 2 types or sub-types ($95.80)*	The methodology, resources, and amount of genetic material sequenced are comparable to that of U0003 (or 87502)