Appendix I

Genetic Testing Code Modifiers

This listing of modifiers is intended for reporting with molecular laboratory procedures related to genetic testing. Genetic testing modifiers should be used in conjunction with CPT and HCPCS codes to provide diagnostic granularity of service to enable providers to submit complete and precise genetic testing information without altering test descriptors. These two-character modifiers are categorized by mutation. The first (numeric) character indicates the disease category and the second (alpha) character denotes gene type. Introductory guidelines in the molecular diagnostic and molecular cytogenetic code sections of the CPT codebook provide further guidance in interpretation and application of genetic testing modifiers.

Neoplasia (Solid Tumor, Excluding Sarcoma and Lymphoma)

0A BRCA1 (hereditary breast/ovarian cancer)

0B BRCA2 (hereditary breast cancer)

0C Neurofibromin (neurofibromatosis, type 1)

0D Merlin (neurofibromatosis, type 2)

0E c-RET (multiple endocrine neoplasia, types 2A/B, familial medullary thyroid carcinoma)

0F VHL (Von Hippel Lindau disease, renal carcinoma)

0G SDHD (hereditary paraganglioma)

0H SDHB (hereditary paraganglioma)

0I ERRB2, commonly called Her-2/neu

0J MLH1 (HNPCC, mismatch repair genes)

0K MSH2, MSH6, or PMS2 (HNPCC, mismatch repair genes)

0L APC (hereditary polyposis coli)

0M Rb (retinoblastoma)

0N TP53, commonly called p53

0O PTEN (Cowden's syndrome)

0P KIT, also called CD117 (gastrointestinal stromal tumor)

0Z Solid tumor gene, not otherwise specified

Neoplasia (Sarcoma)

1A WT1 or WT2 (Wilm's tumor)

1B PAX3, PAX7, or FOXO1A (alveolar rhabdomyosarcoma)

1C FLI1, ERG, ETV1, or EWSR1 (Ewing's sarcoma, desmoplastic round cell)

1D DDIT3 or FUS (myxoid liposarcoma)

1E NR4A3, RBF56, or TCF12 (myxoid chondrosarcoma)

1F SSX1, SSX2, or SYT (synovial sarcoma)

1G MYCN (neuroblastoma)

1H COL1A1 or PDGFB (dermatofibrosarcoma protruberans)

1I TFE3 or ASPSCR1 (alveolar soft parts sarcoma)

1J JAZF1 or JJAZ1 (endometrial stromal sarcoma)

1Z Sarcoma gene, not otherwise specified

Neoplasia (Lymphoid/Hematopoietic)

2A RUNX1 or CBFA2T1, commonly called AML1 or ETO, genes associated with t(8;21) AML1—also ETO (acute myelogenous leukemia)

2B BCR or ABL1, genes associated with t(9;22) (chronic myelogenous or acute leukemia) BCR—also ABL (chronic myeloid, acute lymphoid leukemia)

2C PBX1 or TCF3, genes associated with t(1;19) (acute lymphoblastic leukemia) CGF1

2D CBFB or MYH11, genes associated with inv 16 (acute myelogenous leukemia) CBF beta (leukemia)

2E MLL (acute leukemia)

2F PML or RARA, genes associated with t(15;17) (acute promyelocytic leukemia) PML/RAR alpha (promyelocytic leukemia)

2G ETV6, commonly called TEL, gene associated with t(12;21) (acute leukemia) TEL (Leukemia)

2H BCL2 (B cell lymphoma, follicle center cell origin) bcl-2 (Lymphoma)

2I CCND1, commonly called BCL1, cyclin D1 (Mantle cell lymphoma, myeloma) bcl-1 (lymphoma)

2J MYC (Burkitt lymphoma) c-myc (lymphoma)

2K IgH (lymphoma/leukemia)

2L IGK (lymphoma/leukemia)

2M TRB, T cell receptor beta (lymphoma/leukemia)

2N TRG, T cell receptor gamma (lymphoma/leukemia)

2O SIL or TAL1 (T cell leukemia)

2T BCL6 (B cell lymphoma)

2Q API1 or MALT1 (MALT lymphoma)

2R NPM or ALK, genes associated with t(2;5) (anaplastic large cell lymphoma)

2S FLT3 (Acute myelogenous leukemia)

2Z Lymphoid/hematopoietic neoplasia, not otherwise specified

Non-Neoplastic Hematology/Coagulation

3A F5, commonly called Factor V (Leiden, others) (hypercoagulable state)

3B FACC (Fanconi anemia)

3C FACD (Fanconi anemia)

3D HBB, beta globin (thalassemia, sickle cell anemia, other hemoglobinopathies)

3E HBA, commonly called alpha globin (thalassemia)

3F MTHFR (elevated homocystinemia)

3G F2, commonly called prothrombin (20210, others) (hypercoagulable state) prothrombin (factor II, 20210A) (hypercoagulable state)

3H F8, commonly called factor VIII (hemophilia A/VWF)

3I F9, commonly called factor IX (hemophilia B)

3K F13, commonly called factor XIII (bleeding or hypercoagulable state) beta globin

3Z Non-neoplastic hematology/coagulation, not otherwise specified

Histocompatiblity/Blood Typing/Identity/Microsatellite

▲4A HLA-A*

▲4B HLA-B*

▲4C HLA-C*

(Modifier 4D has been deleted)

▲4E HLA-DRB all

●4P HLA-DRB1*

●4Q HLA-DRB3*

●4R HLA-DRB4*

●4S HLA-DRB5*

●4T HLA-DQA1*

▲4F HLA-DQB1*

#● 4U HLA-DPA1*

▲4G HLA-DPB1*

4H Kell

4I Fingerprint for engraftment (post allogeneic progenitor cell transplant)

4J Fingerprint for donor allelotype (allogeneic transplant)

4K Fingerprint for recipient allelotype (allogeneic transplant)

4L Fingerprint for leukocyte chimerism (allogeneic solid organ transplant)

4M Fingerprint for maternal versus fetal origin

4N Microsatellite instability

4O Microsatellite loss (loss of heterozygosity)

4P Modifier is out of numerical sequence. See Modifier 4A-4Z

4Q Modifier is out of numerical sequence. See Modifier 4A-4Z

4R Modifier is out of numerical sequence. See Modifier 4A-4Z

4S Modifier is out of numerical sequence. See Modifier 4A-4Z

4T Modifier is out of numerical sequence. See Modifier 4A-4Z

4U Modifier is out of numerical sequence. See Modifier 4A-4Z

▲4Z Histocompatiblity/typing, not otherwise specified

Neurologic, Non-Neoplastic

5A ASPA, commonly called Aspartoacylase A (Canavan disease)

5B FMR-1 (fragile X, FRAXA, syndrome)

5C FRDA, commonly called Frataxin (Freidreich ataxia)

5D HD, commonly called Huntington (Huntington's disease)

5E GABRA5, NIPA1, UBE3A, or ANCR GABRA (Prader Willi-Angelman syndrome)

5F GJB2, commonly called Connexin-26 (hereditary hearing loss) Connexin-32 (GJB2) (hereditary deafness)

5G GJB1, commonly called Connexin-32 (X-linked Charcot-Marie-Tooth disease)

5H SNRPN (Prader Willi-Angelman syndrome)

5I SCA1, commonly called Ataxin-1 (spinocerebellar ataxia, type 1)

5J SCA2, commonly called Ataxin-2 (spinocerebellar ataxia, type 2)

5K MJD, commonly called Ataxin-3 (spinocerebellar ataxia, type 3, Machado-Joseph disease)

5L CACNA1A (spinocerebellar ataxia, type 6)

5M ATXN7 Ataxin-7 (spinocerebellar ataxia, type 7)

5N PMP-22 (Charcot-Marie-Tooth disease, type 1A)

5O MECP2 (Rett syndrome)

5Z Neurologic, non-neoplastic, not otherwise specified

Muscular, Non-Neoplastic

6A DMD, commonly called dystrophin (Duchenne/Becker muscular dystrophy)

6B DMPK (myotonic dystrophy, type 1)

6C ZNF-9 (myotonic dystrophy, type 2)

6D SMN1/SMN2 (autosomal recessive spinal muscular atrophy)

6E MTTK, commonly called tRNAlys (myotonic epilepsy, MERRF)

6F MTTL1, commonly called tRNAleu (mitochondrial encephalomyopathy, MELAS)

6Z Muscular, not otherwise specified

Metabolic, Other

7A APOE, commonly called apolipoprotein E (cardiovascular disease or Alzheimer's disease)

7B NPC1 or NPC2, commonly called sphingomyelin phosphodiesterase (Nieman-Pick disease)

7C GBA, commonly called acid beta glucosidase (Gaucher disease)

7D HFE (hemochromatosis)

7E HEXA, commonly called hexosaminidase A (Tay-Sachs disease)

7F ACADM (medium chain acyl CoA dehydrogenase deficiency)

7Z Metabolic, other, not otherwise specified

Metabolic, Transport

8A CFTR (cystic fibrosis)

8B PRSS1 (hereditary pancreatitis)

8C Long QT syndrome, KCN (Jervell and Lange-Nielsen syndromes, types 1, 2, 5, and 6) and SCN (Brugada syndrome, SIDS and type 3)

8Z Metabolic, transport, not otherwise specified

Metabolic-Pharmacogenetics

9A TPMT, commonly called (thiopurine methyltransferase) (patients on antimetabolite therapy)

9B CYP2 genes, commonly called cytochrome p450 (drug metabolism)

9C ABCB1, commonly called MDR1 or p-glycoprotein (drug transport)

9D NAT2 (drug metabolism)

9L Metabolic-pharmacogenetics, not otherwise specified

Dysmorphology

9M FGFR1 (Pfeiffer and Kallman syndromes)

9N FGFR2 (Crouzon, Jackson-Weiss, Apert, Saethre-Chotzen syndromes)

9O FGFR3 (achondroplasia, hypochondroplasia, thanatophoric dysplasia, types I and II, Crouzon syndrome with acanthosis nigricans, Muencke syndromes)

9P TWIST (Saethre-Chotzen syndrome)

9Q DGCR, commonly called CATCH-22 (DiGeorge and 22q11 deletion syndromes)

9Z Dysmorphology, not otherwise specified