Test Specific Guidelines

Epilepsy Genetic Testing

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Procedures Addressed

The inclusion of any procedure code in this table is provided for informational purposes and is not a guarantee of coverage nor an indication that prior authorization is required.

Procedures covered by this guideline	Procedure codes
CACNA1A Full Gene Sequence	81185
CSTB Full Gene Sequence	81189
CSTB Gene Analysis; evaluation to detect abnormal alleles	81188
Epilepsy Gene Analysis	81400 81401 81402 81403 81404 81405 81406 81407 81408 81479
Epilepsy Gene Known Familial Mutation Analysis	81403
Epilepsy Gene 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)	81419
Genomic Unity CACNA1A Analysis	0231U
Genomic Unity CSTB Analysis	0232U

What Is Epilepsy?

Definition

Epilepsy is a neurological condition that causes seizures.

Prevalence

Epilepsy is one of the most common disorders, with an estimated prevalence of 6 in 1000 people worldwide.[1,2]

Symptoms

Epilepsy can manifest in different ways, including different types of seizures or with multiple neurodevelopmental and medical complications besides seizures. Seizure types include generalized seizures (absence seizures, tonic-clonic seizures) and focal seizures (simple focal seizures, complex focal seizures, secondary generalized seizures, among others).

Cause

Epilepsy has multiple causes. These include, but are not limited to, acquired causes such as stroke, brain tumor, head injury, and central nervous system infection.[2] There are also numerous genetic conditions associated with epilepsy. It is estimated that approximately 40% of individuals with seizures have an underlying genetic basis for their condition (see Table 1 for a list of common genetic causes).[3]

Epileptic encephalopathy is a group of disorders in which seizures are accompanied by developmental delays, cognitive impairment, or a host of other neurological issues such as feeding difficulties, sleep dysregulation, and behavioral problems.[4] Knowledge regarding the genetic basis of these disorders has increased significantly in the last decade due to the advent of high throughput Next Generation Sequencing methods, resulting in wider availability of multi-gene panel testing. The following are examples of epileptic encephalopathies:

Ohtahara Syndrome (Early Infantile Epileptic Encephalopathy)

"Characterized by early onset intractable tonic spasms, suppression-burst pattern on interictal EEG, and poor prognosis." [5]

"To date various genes, which have essential roles in the brain's neuronal and interneuronal functions, have been reported to be associated with Ohtahara syndrome. For instance, syntaxin binding protein 1 (STXBP1) regulates synaptic vesicle release [11]; aristaless-related homeobox (ARX) acts as a regulator of proliferation and differentiation of neuronal progenitors [12]; solute carrier family

25 member 22 (SLC25A22) encodes a mitochondrial glutamate transporter13; and potassium voltage-gated channel, KQT-like subfamily, member 2 (KCNQ2) plays a key role in a cell's ability to generate and transmit electrical signals." [6]

Dravet Syndrome (Severe Myoclonic Epilepsy of Infancy)

"Clinical cardinal features include febrile or afebrile generalized or hemiconvulsions starting in the first year of life, seizure evolution to a mixture of intractable generalized (myoclonic or atonic seizures, atypical absences) and focal seizures, normal early development, subsequent psychomotor retardation, and normal brain imaging at onset." [5]

"In most of the cases with Dravet syndrome, one single gene has been involved, in contrast to other epileptic encephalopathy syndromes. SCN1A mutations have been shown in at least 80% of patients with Dravet syndrome." [6]

Infantile Spasms (West Syndrome and X-linked Infantile Spasms)

"West syndrome is characterized by a specific seizure type, i.e., epileptic spasms, a unique interictal EEG pattern termed hypsarrhythmia, and psychomotor retardation. Spasms start within the first year of life, mainly between 4 and 6 months of age." [5]

"There are multiple genetic determinants of infantile spasms, which are usually explained by mutations in distinct genes. Genetic analysis of children with unexplained infantile spasms have demonstrated mutations on the X chromosome in genes such as ARX, cyclin-dependent kinase-like 5 (CDKL5), and UDP-N-acetylglucosaminyltransferase subunit (ALG13) as well as de novo mutations in autosomal genes, including membrane-associated guanylate kinase, WW and PDZ domain containing protein 2 (MAGI2), STXBP1, sodium channel alpha 1 subunit (SCN1A), sodium channel protein type 2 subunit alpha (SCN2A), g-aminobutyric acid (GABA) A receptor, beta 3 (GABRB3), and dynamin 1 (DNM1)." [6]

Epilepsy and Intellectual Disability Limited to Females

"Epilepsy and intellectual disability limited to females (EFMR) is an underrecognized disorder with X-linked inheritance but surprisingly only affecting females while sparing transmitting males. Seizure, cognitive, and psychiatric phenotypes show heterogeneity. Seizures start from the age of 6 to 36 months and may be precipitated by fever. Seizure types include GTCS, myoclonic and tonic seizures, absences, and focal." [5]

"Different mutations of PCDH19 (protocadherin 19), including missense, nonsense, and frameshift mutations, have been reported as the cause of EFMR." [5]

Whole-genome screening for CNVs identifies potentially pathogenic deletions or duplications in ~5% of patients with a range of epilepsy phenotypes, including focal epilepsy, generalized epilepsies, epileptic encephalopathies, fever-associated epilepsy syndromes, and patients with neurodevelopmental disorders and epilepsy.[7]

Inheritance

Inheritance patterns differ between various epilepsy syndromes including dominant, X-linked, recessive, and mitochondrial causes, in addition to epilepsy caused by de novo (or new) genetic mutations. Clinical heterogeneity is also seen in these conditions.

Diagnosis

An electroencephalograph (EEG) can be used to help diagnose epilepsy and possibly give information as to the seizure type. A brain magnetic resonance imaging (MRI) scan can further help define whether epilepsy is caused by a structural brain abnormality or help determine the origin of epilepsy.

Genetic testing for epilepsy is complicated by many factors. Epilepsy syndromes frequently have overlapping features, such as the types of seizures involved and/or additional clinical findings. Many (if not most) epilepsy syndromes, including epileptic encephalopathy, are genetically heterogeneous, and can be caused by mutations in a number of different genes. Sometimes, the inheritance pattern or the presence of pathognomonic features makes the underlying syndrome clear. However, in many cases, it can be difficult to reliably diagnose an epilepsy syndrome based on clinical and family history alone.

NGS-based testing has been shown to dramatically improve the diagnostic rate for children and adults with epilepsy, as well as significantly shorten the time from assessment to diagnosis.[8-10] The diagnostic yield of NGS in patients with epileptic encephalopathies ranges is estimated to be 20-30%.[11,12]

Clinical information (e.g. age of onset, seizure type, EEG results, etc.) or family history may be used in some cases to help narrow down the suspected cause. In these cases, it may be possible to identify a narrow subset of genes that may be responsible for a person's epilepsy.[5,6]

Management

Treatment for epilepsy ranges from antiepileptic drugs (AEDs) to the ketogenic diet to vagal nerve stimulation to epilepsy surgery in the most severe situations. Not all treatments will work for everyone and often, it takes multiple treatment trials to find a regimen that is successful. In a rapidly growing number of epilepsy disorders, knowing the genetic mutation that is responsible for the epilepsy has been shown to help guide management and provide more disease-specific treatment.[13,14]

Survival

Lifespan is dependent upon seizure control and the underlying cause of the individual's epilepsy.

Test Information

Introduction

Genetic testing for epilepsy may consist of next-generation sequencing or multigene panels.

Next Generation Sequencing Assay

Next generation sequencing (NGS), which is also sometimes called massively parallel sequencing, was developed in 2005 to allow larger scale and more efficient gene sequencing. NGS relies on sequencing many copies of small pieces of DNA simultaneously and using bioinformatics to assemble the sequence. Sequence analysis detects single nucleotide substitutions and small (several nucleotide) deletions and insertions. Regions analyzed typically include the coding sequence and intron/exon boundaries. Promoter regions and intronic sequences may also be sequenced if disease-causing mutations are known to occur in these regions of a gene.

Multi-Gene Testing Panels

The efficiency of NGS has led to an increasing number of large, multi-gene testing panels. NGS panels that test several genes at once are particularly well-suited to conditions caused by more than one gene or where there is considerable clinical overlap between conditions making it difficult to reliably narrow down likely causes. Additionally, tests should be chosen to maximize the likelihood of identifying mutations in the genes of interest, contribute to alterations in patient management, and/or minimize the chance of finding variants of uncertain clinical significance.

Guidelines and Evidence

Introduction

This section includes relevant guidelines and evidence pertaining to genetic testing for epilepsy.

Selected Relevant Publications

No current U.S guidelines address the use of multi-gene panels in epilepsy. Peer reviewed and expert authored articles are presented below.

In 2016, a peer reviewed article on genetic testing for epileptic encephalopathy stated the following:

“Second line investigations: Targeted next generation sequencing panels of epileptic encephalopathy genes for individuals with epileptic encephalopathy.” [4]

In 2016, a peer reviewed article on genetic causes of early-onset epileptic encephalopathy stated the following:[6]

“Molecular-based studies on early-onset epileptic encephalopathies should be performed, necessitating programmed genetical algorithms. If the phenotype could be determined with clinical findings, specific gene testing would be helpful

in diagnosis. However, if the phenotype could not be determined because of overlapping phenotypes of different syndromes and the spectrum of phenotypes seen in different mutations, the use of gene panels for epilepsy would increase the probability of correct diagnosis. In a recent study, the rate of diagnosis with targeted single gene sequencing has been reported as 15.4%, whereas the rate has increased to 46.2% with the utility of epilepsy gene panels."

A Task Force for the ILAE Commission of Pediatrics (2015) published recommendations for the management of infantile seizures. These recommendations included the following on treatments:[15]

"for Dravet syndrome, strong evidence supports that stiripentol is effective (in combination with valproate and clobazam), whereas weak evidence supports that topiramate, zonisamide, valproate, bromide, and the ketogenic diet are possibly effective; and for Ohtahara syndrome, there is weak evidence that most antiepileptic drugs are poorly effective."

"Genetic evaluation for Dravet syndrome and other infantile-onset epileptic encephalopathies should be available at tertiary and quaternary levels of care (optimal intervention would permit an extended genetic evaluation) (level of evidence—weak recommendation, level C)"

"Early diagnosis of some mitochondrial conditions may alter long-term outcome, but whether screening at quaternary level is beneficial is unknown (level of evidence U)"

Multiple peer-reviewed articles have shown that epilepsy multi-gene panels have a significant diagnostic yield when seizure onset is in infancy or early childhood.[10,16-18] The diagnostic yields in adults with epilepsy tend to be lower.[19,20]

Criteria

This policy applies to all epilepsy testing, including single gene analysis and multi-gene panels, which are defined as assays that simultaneously test for more than one epilepsy gene. Medical necessity coverage generally relies on criteria established for testing individual genes.

Coverage criteria differ based on the type of testing being performed (i.e., individual epilepsy genes separately chosen versus pre-defined panels of epilepsy genes) and how that testing will be billed (one or more individual epilepsy gene procedure codes, specific panel procedure codes, or unlisted procedure codes).

Epilepsy Single Gene Tests

Epilepsy single gene tests will be covered when the following criteria are met:

The member has a condition that will benefit from information provided by the requested epilepsy gene testing based on at least one of the following criteria:

The member displays clinical features of the condition for which testing is being requested and a particular treatment is being considered for the member that requires a genetic diagnosis, OR

A particular AED is being considered for the member and the AED is contraindicated for individuals with mutations in that gene, defined by ONE of the following criteria:

A neurology therapy FDA label requires results from the genetic test to effectively or safely use or avoidance of the therapy for the member's epilepsy type and the member has not previously had a trial of the therapy, or

An American neurological society specifically recommends the testing for the safe and effective use or avoidance of a therapy and the member has not previously had a trial of the therapy, OR

The member meets all criteria in a test-specific guideline, if available (see Table 1 for a list of genes, associated conditions, and applicable policy), AND

The member does not have a known underlying cause for their seizures (e.g. tumor, head trauma, known genetic condition), AND

Rendering laboratory is a qualified provider of service per the Health Plan policy.

Epilepsy Multi-gene Panels

When separate procedure codes will be billed for individual epilepsy genes (e.g., Tier 1 MoPath codes 81200-81355 or Tier 2 MoPath codes 81400-81408), each individually billed test will be evaluated separately. The following criteria will be applied:

The member has a condition that will benefit from information provided by the requested epilepsy gene testing based on at least one of the following criteria:

The member displays clinical features of the condition for which testing is being requested and a particular treatment is being considered for the member that requires a genetic diagnosis, OR

A particular AED is being considered for the member and the AED is contraindicated for individuals with mutations in that gene by ONE of the following:

A neurology therapy FDA label requires results from the genetic test to effectively or safely use or avoidance the therapy for the member's epilepsy type and the member has not previously had a trial of the therapy, or

An American neurological society specifically recommends the testing for the safe and effective use or avoidance of a therapy and the member has not previously had a trial of the therapy, OR

The member meets all criteria in a test-specific guideline, if available, (see Table 1 for a list of genes, associated conditions, and applicable policy), AND

The member does not have a known underlying cause for their seizures (e.g. tumor, head trauma, known genetic condition), AND

Rendering laboratory is a qualified provider of service per the Health Plan policy.

If the member meets the following criteria, the entire panel will be approved. However, the laboratory will be redirected to use a panel CPT code for billing purposes (e.g. 81419 or 81479):

The member has a diagnosis of early infantile epileptic encephalopathy, OR

The member has a diagnosis of infantile spasms, OR

The member has a diagnosis of intractable, neonatal seizures, OR

The member has a diagnosis of febrile seizures with at least one episode of status epilepticus, OR

The member has a progressive neurological disease defined by the following:

Member has epilepsy with persistent loss of developmental milestones, and

Member's seizures are worsening in severity and/or frequency despite treatment, OR

A particular AED is being considered for the member and there are 2 or more genes on the panel for which the AED is contraindicated for individuals with mutations in that gene by ONE of the following:

A neurology therapy FDA label requires results from the genetic test to effectively or safely use or avoidance the therapy for the member's epilepsy type and the member has not previously had a trial of the therapy, or

An American neurological society specifically recommends the testing for the safe and effective use or avoidance of a therapy and the member has not previously had a trial of the therapy, AND

The member does not display clinical features of a specific condition for which testing is available (e.g. Tuberous Sclerosis, Angelman Syndrome, Rett Syndrome, etc.), AND

The member does not have a known underlying cause for their seizures (e.g. tumor, head trauma, known genetic condition), AND

Rendering laboratory is a qualified provider of service per the Health Plan policy.

When a multi-gene panel is being requested and will be billed with a single panel CPT code (e.g. 81419 or 81479), the panel will be considered medically necessary when the following criteria are met:

The member has a diagnosis of early infantile epileptic encephalopathy, OR

The member has a diagnosis of infantile spasms, OR

The member has a diagnosis of intractable, neonatal seizures, OR

The member has a diagnosis of febrile seizures with at least one episode of status epilepticus, OR

The member has a progressive neurological disease defined by the following:

Member has epilepsy with persistent loss of developmental milestones, and

Member's seizures are worsening in severity and/or frequency despite treatment, OR

A particular AED is being considered for the member and there are 2 or more genes on the panel for which the AED is contraindicated for individuals with mutations in that gene by ONE of the following:

A neurology therapy FDA label requires results from the genetic test to effectively or safely use or avoidance the therapy for the member's epilepsy type and the member has not previously had a trial of the therapy, or

An American neurological society specifically recommends the testing for the safe and effective use or avoidance of a therapy and the member has not previously had a trial of the therapy, AND

The member does not display clinical features of a specific condition for which testing is available (e.g. Tuberous Sclerosis, Angelman Syndrome, Rett Syndrome, etc.), AND

The member does not have a known underlying cause for their seizures (e.g. tumor, head trauma, known genetic condition), AND

Rendering laboratory is a qualified provider of service per the Health Plan policy.

Billing and Reimbursement Considerations

The billed amount should not exceed the list price of the test.

Large epilepsy panels may not be medically necessary when smaller panels are available and are more appropriate based on the clinical findings.

Genetic testing for a specific gene may be necessary only once per lifetime. Therefore, a single gene included in a panel or a multi-gene panel may not be reimbursed if testing has been performed previously. Exceptions may be considered if technical advances in testing demonstrate significant advantages that would support a medical need to retest. Further, given rapidly advancing knowledge regarding genetic variations in epilepsy and in normal or healthy populations, re-analysis of genetic tests may be warranted at regular intervals.

This guideline may not apply to genetic testing for indications that are addressed in test-specific guidelines. Please see the test-specific list of guidelines for a complete list of test-specific panel guidelines.

If a panel was previously performed and an updated, larger panel is being requested, only testing for the medically necessary, previously untested genes will be reimbursable. Therefore, only the most appropriate procedure codes for those additional genes will be considered for reimbursement.

If the laboratory will not accept redirection to a single code, the medical necessity of each billed component procedure will be assessed independently using the criteria above for single gene testing. Only the individual panel components that meet medical necessity criteria as a first tier of testing will be reimbursed. The remaining individual components will not be reimbursable.

Table 1: Common Epilepsy Genes, Associated Conditions and Applicable Guidelines

This is a representative list of known epilepsy genes and is not all inclusive:

Gene	CPT	Condition	Applicable guideline name	Applicable guideline number
ALDH7A1	81406	Pyridoxine-Dependent Epilepsy	Epilepsy Genetic Testing	MOL.TS.257
ARX	81404	ARX-Related Neurodevelopmental Disorders	Epilepsy Genetic Testing	MOL.TS.257
ATP1A2	81406	Familial Hemiplegic Migraine	Epilepsy Genetic Testing	MOL.TS.257
ARGHEF9	81479	ARGHEF9-Related Epilepsy (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
CACNA1A	81185	Familial Hemiplegic Migraine, Episodic Ataxia	Epilepsy Genetic Testing	MOL.TS.257
CDKL5	81406	Infantile Spasms; Early Seizure Variant Rett Syndrome	Epilepsy Genetic Testing	MOL.TS.257
CHD2	81479	CHD2-Related Neurodevelopmental Disorders (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
CHRNA2	81479	ADNFLE	Epilepsy Genetic Testing	MOL.TS.257

Gene	CPT	Condition	Applicable guideline name	Applicable guideline number
CHRNA4	81405	ADNFLE	Epilepsy Genetic Testing	MOL.TS.257
CHRNB2	81405	ADNFLE	Epilepsy Genetic Testing	MOL.TS.257
CLN3	81479	Neuronal Ceroid Lipofuscinosis	Epilepsy Genetic Testing	MOL.TS.257
CLN5	81479	Neuronal Ceroid Lipofuscinosis	Epilepsy Genetic Testing	MOL.TS.257
CLN8	81479	Neuronal Ceroid Lipofuscinosis	Epilepsy Genetic Testing	MOL.TS.257
CNTNAP2	81406	Pitt-Hopkins-Like Syndrome	Epilepsy Genetic Testing	MOL.TS.257
CSTB*	81188 81189 81190	PME (Unverrict-Lundborg)	Epilepsy Genetic Testing	MOL.TS.257
DEPDC5	81479	DEPDC5-Related Epilepsy	Epilepsy Genetic Testing	MOL.TS.257
EFHC1	81406	Susceptibility to Juvenile Absence & Myoclonic Epilepsies	Epilepsy Genetic Testing	MOL.TS.257
EPM2A	81404	PME (Lafora Disease)	Epilepsy Genetic Testing	MOL.TS.257
FOLR1	81479	Cerebral Folate Transport Deficiency	Epilepsy Genetic Testing	MOL.TS.257
FOXG1	81404	Congenital Variant Rett Syndrome	Epilepsy Genetic Testing	MOL.TS.257
GABRA1	81479	GABRA1-Related Epilepsy (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257

Gene	CPT	Condition	Applicable guideline name	Applicable guideline number
GABRB3	81479	GABRB3-Related Epilepsy (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
GABRG2	81405	GABRG2-Related Epilepsy (GEFS+ included)	Epilepsy Genetic Testing	MOL.TS.257
GAMT	81479	Creatine Deficiency Syndromes	Epilepsy Genetic Testing	MOL.TS.257
GATM	81479	Creatine Deficiency Syndromes	Epilepsy Genetic Testing	MOL.TS.257
GRIN2A	81479	GRIN2A-Related Speech Disorders & Epilepsy (Landau-Kleffner included)	Epilepsy Genetic Testing	MOL.TS.257
KCNJ10	81404	EAST/SeSAME Syndrome	Epilepsy Genetic Testing	MOL.TS.257
KCNQ2	81406	KCNQ2-Related Disorders (BFNS & EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
KCNQ3	81479	KCNQ3-Related Disorders (BFNS included)	Epilepsy Genetic Testing	MOL.TS.257
KCNT1	81479	KCNT1-Related Disorders (ADNFLE & EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
KCTD7	81479	PME With or Without Inclusions, Neuronal Ceroid Lipofuscinosis	Epilepsy Genetic Testing	MOL.TS.257
LGI1	81479	Autosomal Dominant Partial Epilepsy with Auditory Features	Epilepsy Genetic Testing	MOL.TS.257

Gene	CPT	Condition	Applicable guideline name	Applicable guideline number
MBD5	81479	MBD5 Haploinsufficiency	Epilepsy Genetic Testing	MOL.TS.257
MECP2	81302	Classic Rett Syndrome; MECP2-Related Epileptic Encephalopathy (males)	Rett Syndrome Testing	MOL.TS.224
MEF2C	81479	Intellectual disability, Stereotypic Movements, Epilepsy, and/or Cerebral Malformations	Epilepsy Genetic Testing	MOL.TS.257
NHLRC1	81403	PME (Lafora Disease)	Epilepsy Genetic Testing	MOL.TS.257
NRXN1	81479	Pitt-Hopkins-Like Syndrome	Epilepsy Genetic Testing	MOL.TS.257
PCDH19	81405	Epilepsy & Intellectual Disability Limited to Females	Epilepsy Genetic Testing	MOL.TS.257
PNKP	81479	PNKP-Related Epilepsy (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
PNPO	81479	Pyridoxamine 5'-Phosphate Oxidase Deficiency	Epilepsy Genetic Testing	MOL.TS.257
POLG	81406	POLG-Related Disorders (Alpers Syndrome included)	Epilepsy Genetic Testing	MOL.TS.257
PRICKLE1	81479	PME	Epilepsy Genetic Testing	MOL.TS.257
PPT1	81479	Neuronal Ceroid Lipofuscinosis	Epilepsy Genetic Testing	MOL.TS.257

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Gene	CPT	Condition	Applicable guideline name	Applicable guideline number
PRRT2	81479	PRRT2-Related Disorders	Epilepsy Genetic Testing	MOL.TS.257
SCARB2	81479	Action Myoclonus-Renal Failure Syndrome; PME	Epilepsy Genetic Testing	MOL.TS.257
SCN1A	81407	SCN1A-Related Disorders (Dravet syndrome & GEFS+ included)	Epilepsy Genetic Testing	MOL.TS.257
SCN1B	81404	SCN1B-Related Disorders (GEFS+ & EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
SCN2A	81479	SCN2A-Related Disorders (BFIS & EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
SCN8A	81479	SCN8A-Related Disorders (BFIS & EOEE Included)	Epilepsy Genetic Testing	MOL.TS.257
SLC19A3	81479	Biotin-Thiamine-Responsive Basal Ganglia Disease	Epilepsy Genetic Testing	MOL.TS.257
SLC2A1	81405	GLUT1 Deficiency	Epilepsy Genetic Testing	MOL.TS.257
SLC25A22	81479	SLC25A22-Related Epilepsy (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
SLC9A6	81406	Christianson Syndrome	Epilepsy Genetic Testing	MOL.TS.257
SPTAN1	81479	SPTAN1-Related Epilepsy (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257

Gene	CPT	Condition	Applicable guideline name	Applicable guideline number
STXBP1	81406	STXBP1-Related Disorders (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
TBC1D24	81479	TBC1D24-Related Disorders (EOEE included)	Epilepsy Genetic Testing	MOL.TS.257
TCF4	81406	Pitt-Hopkins Syndrome	Epilepsy Genetic Testing	MOL.TS.257
TSC1	81406	Tuberous Sclerosis	Epilepsy Genetic Testing	MOL.TS.257
TSC2	81407	Tuberous Sclerosis	Epilepsy Genetic Testing	MOL.TS.257
TPP1	81479	Neuronal Ceroid Lipofuscinosis	Epilepsy Genetic Testing	MOL.TS.257
UBE3A	81406	Angelman Syndrome	Angelman Syndrome Testing	MOL.TS.126
ZEB2	81405	Mowat-Wilson Syndrome	Epilepsy Genetic Testing	MOL.TS.257

Note ***90% of Unverrict-Lundborg syndrome is due to a repeat expansion in CSTB that may not be detected using next-generation sequencing and requires specific testing for repeat expansions.**

ADNFLE = Autosomal Dominant Frontal Lobe Epilepsy; BFIS = Benign Familial Infantile Seizures; BFNS = Benign Familial Neonatal Seizures; EOEE = Early-Onset Epileptic Encephalopathy; GEFS+ = Generalized Epilepsy with Febrile Seizures Plus; PME = Progressive Myoclonic Epilepsy

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