MEDICAL POLICY

POLICY TITLE	GENERAL APPROACH TO EVALUATING THE UTILITY OF GENETIC PANELS
POLICY NUMBER	MP-2.323

Original Issue Date (Created):	**11/26/2013**
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I. POLICY

NOTE: This policy applies only if there is no separate medical policy that outlines specific criteria for testing. If a separate policy does exist, then the criteria for medical necessity in that policy supersede the guidelines in this policy.

Additional new products may become commercially available. This is not meant to be a comprehensive list of all available products or tests.

Genetic panels that use next generation sequencing or chromosomal microarray, and are classified in one of the categories below, may be considered **medically necessary** when all criteria are met for each category, as outlined in the Rationale section:

- Panels for hereditary or genetic conditions
  - Diagnostic testing of an individual's germline to benefit the individual
  - Testing of an asymptomatic individual to determine future risk of disease
- Cancer panels
  - Testing of an asymptomatic individual to determine future risk of cancer
  - Testing cancer cells from an individual to benefit the individual by identifying targeted treatment
- Reproductive panels
  - Preconception testing
    - Carrier testing of the parent(s)
  - Prenatal testing
    - Carrier testing of the parent(s)
    - In utero testing of a fetus, including testing for aneuploidy or variants
  - Preimplantation genetic testing.

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***NOTE:** For coverage of CancerNext™, BreastNext™, ColoNext™, OvaNext™ and any other cancer susceptibility panels using next generation sequencing refer to MP-2.325, Genetic Cancer Susceptibility Panels Using Next Generation Sequencing.

Genetic panels that use next generation sequencing or chromosomal microarray that do not meet the criteria for a specific category are considered **investigational** as there is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

POLICY GUIDELINES:

Genetics Nomenclature Update

The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical policy updates starting in 2017 (see Table PG1). The Society's nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—"pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign"—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

Previous	Updated	Definition
Mutation	Diseased-Assoc.Variant	Disease-associated change in the DNA sequence.
	Variant	Change in DNA sequence
	Familial Variant	Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives.

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

Variant Classification	Definition
Pathogenic	Disease-causing change in the DNA sequence
Likely Pathogenic	Likely disease-causing change in the DNA sequence
Variant of uncertain significance	Change in DNA sequence with uncertain effects on disease
Likely benign	Likely benign change in the DNA sequence
Benign	Benign change in the DNA sequence

American College of Medical Genetics and Genomics; AMP: Association of Molecular Pathology.

Genetic Counseling

Experts recommend formal genetic counseling for patients who are at-risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

Cross-references:

MP-2.326 General Approach to Genetic Testing
MP-2.325 Genetic Cancer Susceptibility Panels Using Next Generation Sequencing
MP-2.259 Expanded Molecular Panel Testing of Cancers to Identify Targeted Therapies
MP-7.009 Preimplantation Genetic Testing

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital BlueCross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO: Refer to FEP Benefit Brochure for information on Genetic Testing:
https://www.fepblue.org/benefit-plans/benefit-plans-brochures-and-forms
Note* - The Federal Employee Program (FEP) Service Benefit Plan does not have a medical policy related to these services. “

III. DESCRIPTION/BACKGROUND

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Purpose

The purpose of this policy is to provide a framework for evaluating the utility of genetic panels that use newer genetic testing methodologies. In providing a framework for evaluating genetic panels, this review will not attempt to determine the clinical utility of genetic testing for specific disorders per se. For most situations, this will mean that at least 1 variant in the panel has already been determined to have clinical utility and that clinical indications for testing are established. Once the clinical utility for at least one of the variants included in the panel has been established, then the focus is on whether the use of a panel is a reasonable alternative to individual tests.

Genetic Panel Testing

A genetic panel will be defined as a test that simultaneously evaluates multiple genes, as opposed to sequential testing of individual genes. This includes panels performed by next-generation sequencing (NGS), massive parallel sequencing, and chromosomal microarray analysis. The definition of a panel will not include panels that report on gene expression profiling, which generally do not directly evaluate genetic variants.

New Sequencing Technologies

New genetic technology, such as NGS and chromosomal microarray, has led to the ability to examine many genes simultaneously.[1] This in turn has resulted in a proliferation of genetic panels. Panels using next-generation technology are currently widely available, covering a broad range of conditions related to inherited disorders, cancer, and reproductive testing.[2-4] These panels are intuitively attractive to use in clinical care because they can analyze multiple genes more quickly and may lead to greater efficiency in the workup of genetic disorders. It is also possible that newer technology can be performed more cheaply than direct sequencing, although this may not be true in all cases.

Newer sequencing techniques were initially associated with higher error rates than direct sequencing.[5] While there are limited published data directly comparing the accuracy of NGS with direct sequencing, several publications have reported that the concordance between NGS and Sanger sequencing is greater than 99% for cancer susceptibility testing,[6] inherited disorders,[7] and hereditary hearing loss.[8] Another potential pitfall is the easy availability of a multitude of genetic information, much of which has uncertain clinical consequences. Variants of uncertain significance are found commonly and in greater numbers with NGS than with direct sequencing.[9,10]

The intended use for these panels is variable, for example, for the diagnosis of hereditary disorders, a clinical diagnosis may be already established, and genetic testing is performed to determine whether this is a hereditary condition, and/or to determine the specific variant present. In other cases, there is a clinical syndrome (phenotype) with a broad number of potential diagnoses, and genetic testing is used to make a specific diagnosis. For cancer panels, there are also different intended uses. Some panels may be intended to determine whether a known cancer is part of a hereditary cancer syndrome. Other panels may include somatic variants in a tumor biopsy specimen that may help identify a cancer type or subtype and/or help select the best treatment.

There is no standardization to the makeup of genetic panels. Panel composition is variable, and different commercial products for the same condition may test a different set of genes. The makeup of the panels is determined by the specific lab that developed the test. Also, the composition of any individual panel is likely to change over time, as new variants are discovered and added to existing panels.

Despite the variability in the intended use and composition of panels, there are a finite number of broad panel types that can be identified and categorized. Once categorized, specific criteria on the utility of the panel can be developed for each category. One difficulty with this approach is

that the distinction between the different categories, and the distinction between the intended uses of the panels, may not be clear. Some panels will have features or intended uses that overlap among the different categories.

To determine the criteria used for evaluating panels, the policy will first classify panels into a number of clinically relevant categories, according to their intended use. Then, for each category, criteria will be proposed that can be applied to tests within that category. Because our goal is to outline a general approach to testing, we will not evaluate individual panels; rather, we will supply examples of genetic panels in each category to assist Plans in classifying the individual panels.

REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

An exhaustive list of commercially available panel tests is impractical. For example, the EGL Genetics offers 243 different genetic panels, of a total of 929 molecular genetics tests.[11] Table 1 provides a sample of panels that use NGS or chromosomal microarray technologies.

Table 1. Panels Using Next-Generation Sequencing or Chromosomal Microarray Technology (as of December 2017)

Test Name	Laboratory
Agammaglobulinemia Panel	ARUP Laboratories
Ashkenazi Jewish Diseases Panel	ARUP Laboratories
Mitochondrial Disorders Panel	ARUP Laboratories
Amyotrophic Lateral Sclerosis Pane	ARUP Laboratories
Aortopathy Panel	ARUP Laboratories
Autism Panel	ARUP Laboratories
Brugada Syndrome Panel	ARUP Laboratories
Vascular Malformation Syndromes	ARUP Laboratories
Retinitis Pigmentosa/Leber Congenital Amaurosis Panel	ARUP Laboratories
Cardiomyopathy and Arrhythmia Panel	ARUP Laboratories
Periodic Fever Syndromes Panel	ARUP Laboratories
Arrhythmias Sequencing Panel	EGL Genetics
Arrhythmias Deletion/Duplication Panel	EGL Genetics
Autism Spectrum Disorders	EGL Genetics
Cardiomyopathy Panel	EGL Genetics
Ciliopathies Panel	EGL Genetics
Congenital Glycosylation Disorders	EGL Genetics
ACOG/ACMG Carrier Screen Targeted Mutation Panel	EGL Genetics
Epilepsy	EGL Genetics
Eye Disorders	EGL Genetics

Neuromuscular Disorders	EGL Genetics
Noonan Syndrome and Related Disorders	EGL Genetics
Short Stature Panel	EGL Genetics
Sudden Cardiac Arrest Panel	EGL Genetics
X-linked Intellectual Disability	EGL Genetics
CancerNext™	Ambry Genetics
BreastNext™	Ambry Genetics
ColoNext™	Ambry Genetics
OvaNext™	Ambry Genetics
RhythmNext®	Ambry Genetics
X-linked Intellectual Disability	Ambry Genetics
TAADNext®	Ambry Genetics
Cobalamin Metabolism Comprehensive Panel	Baylor College of Medicine
Progressive External Ophthalmoplegia Panel	Baylor College of Medicine
CoQ10 Comprehensive Panel	Baylor College of Medicine
Usher Syndrome Panel	Baylor College of Medicine
Retinitis Pigmentosa Panel	Baylor College of Medicine
Pyruvate Dehydrogenase Deficiency and Mitochondrial Respiratory Chain Complex V Deficiency Panel	Baylor College of Medicine
Myopathy/Rhabdomyolysis Panel	Baylor College of Medicine
Mitochondrial Disorders Panel	Baylor College of Medicine
Low Bone Mass Panel	Baylor College of Medicine
Glycogen Storage Disorders Panel	Baylor College of Medicine
Leigh Disease Panel	Medical Neurogenetics
Pan Cardiomyopathy Panel	Partners Healthcare
Isolated Non-syndromic Congenital Heart Defects Panel	Partners Healthcare
Noonan Spectrum Panel	Partners Healthcare
Usher Syndrome Panel	Partners Healthcare
Hereditary Colon Cancer Syndromes	Mayo Medical Laboratories
Hypertrophic Cardiomyopathy Panel	Mayo Medical Laboratories
Dilated Cardiomyopathy Panel	Mayo Medical Laboratories
Arrhythmogenic Right Ventricular Cardiomyopathy Panel	Mayo Medical Laboratories
Noonan Syndrome Panel	Mayo Medical Laboratories
Marfan Syndrome Panel	Mayo Medical Laboratories
Long QT Syndrome	Mayo Medical Laboratories
Brugada Syndrome	Mayo Medical Laboratories
Signature Prenatal Microarray	Signature Genomics
Counsyl™ Panel	Counsyl Genomics

IV. RATIONALE

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TYPES OF PANEL TESTING

There are numerous types of panel testing, because in theory a panel may be substituted for individual variant testing in any situation where more than 1 gene is being examined. Commercially available panels fall largely into several categories, which we classify using the BCBSA categories of genetic testing (see Appendix Table 1).

We have classified genetic panels into 3 major categories: panels for genetic and hereditary conditions, cancer panels, and reproductive panels. Within these categories, we created subcategories by the intended use of the panels.

Panels for Genetic or Hereditary Conditions

Panels for genetic or hereditary conditions are generally single-gene disorders, which are inherited in Mendelian fashion. They are defined by a characteristic phenotype, which may characterize a specific disease or represent a syndrome that encompasses multiple underlying diseases.

The intended use of these panels may be for:

- Diagnostic testing of an individual's germline to benefit the individual. To confirm a suspected diagnosis in patients with signs and/or symptoms of the condition; or to identify a causative etiology for a clinical syndrome, for which there are multiple possible underlying conditions.
- Testing an asymptomatic individual to determine future risk of disease.

There are several variations of panels for use in diagnosis or risk assessment of genetic or hereditary conditions. For our purposes, panels will be divided into the following types:

- *Panels containing variants associated with a single condition.* These panels generally include all known pathogenic variants for a defined disease and do not include variants associated with other diseases. An example of such a panel would be one that includes pathogenic variants for hypertrophic cardiomyopathy but does not include variants associated with other cardiovascular disorders. These panels can be used for diagnostic or risk assessment purposes.
- *Panels containing variants associated with multiple related conditions.* These panels include all known pathogenic variants for a defined disease and variants associated with other related disorders. An example of such a panel would be a pan cardiomyopathy panel that includes pathogenic variants for hypertrophic cardiomyopathy and other types of cardiomyopathy (e.g., dilated cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy). These panels can be used for diagnostic or risk assessment purposes.
- *Panels containing variants for clinical syndromes associated with multiple distinct conditions.* These panels include variants associated with multiple potential disease states that define a particular clinical syndrome. In general, a specific diagnosis cannot be made without genetic testing, and genetic testing can identify one among several underlying disease states that manifest as a clinical syndrome. An example of this type of panel is one for intellectual disability that includes variants associated with many potential underlying disease states. These panels are used for diagnostic purposes.

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Cancer Panels

Genetic panels for cancer can be of several types and may test for either germline or somatic variants. Their intended purpose can be for:

- Testing an asymptomatic patient to determine future risk of cancer
- Therapeutic testing of cancer cells from an affected individual to benefit the individual by directing targeted treatment based on specific somatic variants.

There are variations of panels for use in risk assessment or for directing targeted treatment. For our purposes, panels will be divided into the following types:

- *Panels containing multiple variants indicating risk for a specific type of cancer or cancer syndrome (germline variants).* These panels contain multiple related variants that indicate susceptibility to one or more cancers. They include germline variants and will generally be used for risk assessment in asymptomatic individuals who are at-risk for variants based on family history or other clinical data. An example of this type of panel would be one testing for multiple *BRCA1* and *BRCA2* variants associated with hereditary breast and ovarian cancer syndrome.
- *Panels containing multiple variants associated with a wide variety of cancer types (somatic variants).* These panels are generally used to direct treatment with drugs that target specific variants. They test for somatic variants from tissue samples of existing cancers. Many of these somatic variants are found across a wide variety of solid tumors. An example is the CancerNext Panel (Ambry Genetics), which tests for a broad number of somatic variants that can direct treatment.

Reproductive Panels

Reproductive panels test for variants associated with heritable conditions and are intended either for:

- Carrier testing of parent(s) preconception
- Carrier testing of parent(s) prenatal
- Prenatal (in utero) testing

Preconception testing usually tests for variants that are autosomal recessive or X-linked or, in some cases, for autosomal dominant variants with late clinical onset. Preconception tests can be performed on parents at-risk for a variant based on family history or can be done as screening tests in parents without a family history suggestive of a variant. Prenatal testing refers to tests performed during pregnancy. At present, prenatal testing for genetic variants is performed on the fetus, using amniocentesis or chorionic villous sampling. Testing of maternal blood for chromosomal aneuploidy is currently available, and in the future, it may be possible to test for fetal variants using maternal blood.

There are variations of panels for use in preconception or prenatal testing. For our purposes, panels will be divided into the following types:

- *Panels containing variants associated with a single disorder.* These panels are generally performed in at-risk individuals with a family history of a heritable disorder. An example of this type of panel would be a cystic fibrosis gene panel intended for use in individuals with a family history of cystic fibrosis.
- *Panels containing variants associated with multiple disorders.* These panels are generally performed as screening tests for parents without a family history of a heritable disorder. They can also be used to evaluate individuals with a family history of a heritable disorder. An example of this type of panel is the Signature Prenatal Microarray Panel.

Criteria for Evaluating Genetic Panels

The following are criteria that can be applied to evaluating genetic panels, with an explanation of the way the criteria are to be defined and applied. Not all criteria will apply to all panels. Appendix Table 2 and Appendix Figures 1 through 4 list the specific criteria that should be used for each category.

Test Is Performed in a Clinical Laboratory Improvement Amendments–Licensed Lab

- Testing is performed in a laboratory licensed under Clinical Laboratory Improvement Amendments for high-complexity testing. This requires delivery of a reproducible set of called, quality-filtered variants from the sequencing platform.
- These calculations should occur before variant annotation, filtering, and manual interpretation for patient diagnosis.

Technical Reliability of Panels Approaches That of Direct Sequencing

- The technical reliability for detecting individual variants, compared with the criterion standard of conventional direct Sanger sequencing, is reported.
  - The testing methods are described, and the overall analytic validity for that type of testing is defined.
- Any decrease in analytic sensitivity and specificity is not large enough to result in a clinically meaningful difference in diagnostic accuracy (clinically valid).

All individual components of the panel have demonstrated they are clinically useful for the condition being evaluated OR the implications and consequences of test results that have not demonstrated clinical utility are clear, AND there is no potential for incidental findings to cause harm.

- For each panel, if each variant in the panel would be indicated for at least some patients with the condition, then this criterion is met.
  - If there are individual variants that do not have clinical utility, then the potential to cause harm might occur.
- For incidental findings, the potential for harm may be due to:
  - Incorrect diagnosis due to false-positive or false-negative results
    - False-positive: Unnecessary treatment that may have adverse events
    - False-negative: Effective treatment not provided
  - Incorrect risk assessment

- Unnecessary surveillance tests may lead to further confirmatory tests that may be invasive
- Effective surveillance or screening not provided to patients at-risk
- Incorrect decision made on reproductive decision making
  - Alteration made in reproductive planning that would not have been made with correct information
  - No alteration made in reproductive planning, where alteration would have been made with correct information

Panel Testing Offers Substantial Improvement in Efficiency vs Sequential Analysis of Individual Genes

- The composition of the panel is sufficiently complex such that next-generation sequencing or chromosomal microarray analysis is expected to offer considerable advantages. The complexity of testing can be judged by:
  - The number of genes tested.
  - The size of the genes tested.
  - The heterogeneity of the genes tested.

The Impact of Ancillary Information Is Well-Defined

- If a panel contains both variants that are medically necessary and variants that are investigational (or not medically necessary), the impact of results for investigational (or not medically necessary) variants is considered, taking into account the following possibilities:
  - The information may be ignored (no further impact).
  - The information may result in further testing or changes in management:
    - Positive impact
    - Negative impact
  - It is more likely that the results of tests that are not medically necessary cause a negative, rather than a positive, impact on the patient. This is because additional tests and management changes that follow are not evidence-based and because additional testing and treatment generally involve risks.

Decision Making Based on Genetic Results Is Well-Defined

- Results of the genetic testing will lead to changes in diagnosis and/or treatment.
- The potential changes in treatment are defined prior to testing and accord with the current standard of care.
- Changes in diagnosis or management are associated with improvements in health outcomes.
- For prenatal and preconception testing:
  - Alterations in reproductive decision making are expected, depending on the results of testing.

Testing Yield Is Acceptable for the Target Population

- The number of individuals who are found to have a pathogenic variant, in relation to the total number of individuals tested, is reasonable given the underlying prevalence and severity of the disorder, and the specific population that is being tested.
  - It is not possible to set an absolute threshold for acceptable yield across different clinical situations. Some guidance can be given from clinical precedence as follows:
    - For diagnosis of hereditary disorders, genetic testing is generally performed when signs and symptoms of the disease are present, including family history. The likelihood of a positive genetic test depends on the accuracy of the signs and symptoms (pretest probability of disorder), and the clinical sensitivity of genetic testing. For disorders such as testing for congenital long QT syndrome and Duchenne muscular dystrophy, the likelihood of a positive result in patients with signs and symptoms of the disease is greater than 10%.
    - For cancer susceptibility, testing is recommended for genetic abnormalities such as the *BRCA* gene and Lynch syndrome when the likelihood of a positive result is in the range of 2% to 10%.
    - For a clinical syndrome that has multiple underlying etiologies, such as developmental delay in children, chromosomal microarray analysis is recommended when the likelihood of a positive result is in the 5% to 20% range.
- There is an increase in yield over alternative methods of diagnosis, and this increase is clinically significant.

Other Issues to Consider

- Most tests will not, and possibly should not, be ordered by generalists.
  - Guidance for providers is appropriate on the expertise necessary to ensure that test ordering is done optimally.
- Many tests, particularly those for inherited disorders, should be accompanied by patient counseling, preferably by certified genetic counselors.
  - Counseling may be needed both before and after testing, depending on the specific condition being tested.

SUMMARY OF EVIDENCE

Genetic panels using next-generation technology or chromosomal microarray analysis are available for many clinical conditions. The major advantage of panels is the ability to analyze many genes simultaneously, potentially improving the breadth and efficiency of the genetic workup. A potential disadvantage of panels is that they provide a large of amount of ancillary information whose significance may be uncertain. Limited published evidence has reported that the analytic validity of panels approaches that of direct sequencing. The clinical validity and clinical utility of panels are condition-specific. The clinical validity of panels will reflect the clinical validity of the underlying individual variants. The clinical utility of panels will depend on the context in which they are used, ie, whether the advantages of panel testing outweigh the disadvantages for the specific condition under consideration.

V. DEFINITIONS

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N/A

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital BlueCross. Members and providers should consult the member's health benefit plan for information or contact Capital BlueCross for benefit information.

VII. DISCLAIMER

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Capital BlueCross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital BlueCross' Provider Services or Member Services. Capital BlueCross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Codes 81410-81471 are specific CPT codes for genomic sequencing procedures (or "next generation sequencing" panels). The panel must meet the requirements in the code descriptor in order to use the code.

If the panel does not meet the requirements for the codes above and does not utilize an algorithmic analysis, for any specific analyte in the panel that is listed in the Tier 1 (81105-81383) or Tier 2 (81400- 81408) codes that CPT code would be reported for that specific analyte along with the unlisted code 81479 (1 unit) for any analytes on the panel that are not listed in the CPT codes. If none of the analytes on the panel are listed in the more specific CPT codes, unlisted code 81479 would be reported once for the whole test.

If the panel utilizes an algorithmic analysis of the results of the component tests to produce a numeric score or probability, it would be a multianalyte assay with algorithm analysis (MAAA) and reported with one of the specific codes in the 815XX section or appendix O in CPT. If there is no specific code listed, the unlisted MAAA code 81599 would be used.

AMA Proprietary Laboratory Analyses (PLA) codes, 0001U to 0153U, are subject to the above criteria as appropriate.

IX. REFERENCES

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X. POLICY HISTORY

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MP 2.323	**CAC 11/26/13 New policy**. BCBSA adopted. Panels using next generation technology are medically necessary when criteria are met for each category of panels.
	CAC 11/25/14 Consensus review. No change to policy statements. Added clarification – additional new products may become commercially available. This is not meant to be a comprehensive list of all available products or tests. Coding reviewed.
	01/2015- Admin update. New 2015 CPT codes added to policy.
	CAC 11/24/15 Minor review. Wording of policy statement revised to correspond with BCBSA genetic testing categories. Updated rationale and references. Coding reviewed. Updated to include 2016 codes.
	CAC 11/29/16 Consensus review. No change to policy statements. References updated. Coding reviewed. Variation reformatting.
	CAC 11/28/17 Consensus review. No change to policy statements. References updated. Coding reviewed, tier 1 molecular pathology range updated to include new codes effective 1/1/18.
	8/17/18 Consensus review with administrative change. Policy statements unchanged. Policy revised with updated genetics nomenclature; mutation to variant. Description/Background, Rationale and Reference sections updated.
	5/29/2019 Consensus review. Policy statements unchanged. Corrected formatting of tables. References updated. Appendix removed. AMA Proprietary Laboratory Analyses (PLA) codes updated to include codes issued 7/1/19: 0001U to 0104U.
	1/1/2020 Admin update. Removed deleted code 0104U. Added new code 0152U & 0153U.
	5/11/20 Consensus review. Policy statements unchanged.

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