Genetic Panel Testing (5-50 genes) for Hematolymphoid Neoplasms or Disorders

Effective: January 1, 2018

Next Review: November 2018
Last Review: December 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Targeted multiplex genetic sequence analysis panels using DNA/RNA analysis for hematolymphoid neoplasms or disorders comprised of at least five and up to 50 genes may be used to confirm a diagnosis when the genes included have clear clinical utility.

MEDICAL POLICY CRITERIA

Note: This policy addresses genetic panel testing for hematolymphoid neoplasms or disorders. Refer to Evaluating the Utility of Genetic Panels, Genetic Testing, No. 64 for genetic testing panels not listed in this policy.

I) The following genetic panel tests may be considered medically necessary:
   A) MPN Targeted Profile Panel (Genoptix)
   B) Next-Generation Sequencing, Acute Myeloid Leukemia, 8-Gene Panel (Mayo Clinic)

II) When there is not enough research to show that a gene and/or gene variant in a genetic panel test may be used to manage treatment decisions and improve net health outcomes, then the entire genetic panel test is considered investigational, including but not limited to the following:
   A) Myeloid Molecular Profile panel (Genoptix)
B) GeneTrails AML MDS Genotyping panel (Oregon Health and Science University)
C) Hematological Malignancy Mutation Panel (Baylor Genetics)
D) Targeted Cancer Gene Panel (Tricore Reference Laboratories)

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

In order to determine the clinical utility of gene test(s), all of the following information must be submitted for review:

1. Name of the genetic test(s) or panel test
2. Name of the performing laboratory and/or genetic testing organization (more than one may be listed)
3. The exact gene(s) and/or mutation(s) being tested
4. Relevant billing codes
5. Brief description of how the genetic test results will guide clinical decisions that would not otherwise be made in the absence testing
6. Medical records related to this genetic test, if available:
   - History and physical exam
   - Conventional testing and outcomes
   - Conservative treatment provided

CROSS REFERENCES

1. Genetic and Molecular Diagnostic Testing, Genetic Testing, No. 20
2. Genetic Testing for Myeloid Neoplasms and Leukemia, Genetic Testing, No. 59
3. Evaluating the Utility of Genetic Panels, Genetic Testing, No. 64

BACKGROUND

GENETICS NOMENCLATURE UPDATE

Human Genome Variation Society (HGVS) nomenclature[^1] is used to describe variants found in DNA and serves as an international standard. It is being implemented for genetic testing medical evidence review updates starting in 2017. According to this nomenclature, the term “variant” is used to describe a change in a DNA or protein sequence, replacing previously-used terms, such as “mutation.” Pathogenic variants are variants associated with disease, while benign variants are not. The majority of genetic changes have unknown effects on human health, and these are referred to as variants of uncertain significance.

GENETIC PANEL TESTING

Numerous genetic pathogenic variants are associated with various hematolymphoid neoplasms or disorders. Modern genetic technology, such as next-generation sequencing and chromosomal microarray, has led to the ability to examine many genes simultaneously. Some patients may have clinical symptoms for more than one neoplasm or disorder, and it has been proposed that genetic testing using next-generation sequencing technology to analyze multiple genes at a single time point (panel testing) can optimize testing in these patients, as compared to testing one mutation at a time.
Panels using next generation technology are currently available in the areas of cancer, cardiovascular disease, neurologic disease, psychiatric conditions, and for reproductive testing. These panels are intuitively attractive to use in clinical care because they can screen for numerous variants within a single or multiple genes quickly, and may lead to greater efficiency in the work-up of genetic disorders. It is also possible that these “bundled” gene tests can be performed more cost effectively than direct sequencing, although this may not be true in all cases. However, panel testing can also provide information on genetic variants that are of unclear clinical significance or which would not lead to changes in patient management.

One potential challenge of genetic panel testing is the availability of a large amount of ancillary genetic information, much of which there are uncertain clinical consequences and management strategies. Identification of genetic variants for which the clinical management is uncertain may lead to unnecessary follow-up testing and procedures, all of which have their own inherent risks.

Additionally, the design and composition of genetic panel tests have not been standardized. Composition of the panels is variable, and different commercial products for the same condition may test different sets of genes. The make-up of the panel is determined by the specific lab that has developed the test. In addition, the composition of any individual panel is likely to change over time, as new mutations are discovered and added to the existing panels.

HEMATOLYMPHOID NEOPLASMS

Hematolymphoid neoplasms include myeloid neoplasm and acute leukemia which have been classified in a collaboration with the Society for Hematopathology and the European Association for Haematopathology, and published by the World Health Organization (WHO).[2]

Myeloid neoplasm and acute leukemia classification is categorized as nine major groups. Some of the larger categories include, myeloproliferative neoplasms (MPN); myeloid/lymphoid neoplasms with eosinophilia and rearrangement of PDGFRA, PDGFRB, or FGFR1, or with PCM1-JAK2; myelodysplastic/myeloproliferative neoplasms (MDS/MPN); myelodysplastic syndromes (MDS); and acute myeloid leukemia (AML) and related neoplasms.

GENETIC COUNSELING

Due to the complexity of interpreting genetic test results, patients should receive pre- and post-test genetic counseling from a qualified professional when testing is performed to diagnose or predict susceptibility for inherited diseases. The benefits and risks of genetic testing should be fully disclosed to individuals prior to testing, and counseling concerning the test results should be provided.

REGULATORY STATUS

The majority of genetic panel tests are laboratory derived tests that are not subject to U.S. Food and Drug Administration (FDA) approval. Clinical laboratories may develop and validate tests in-house (“home-brew”) and market them as a laboratory service; such tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA). The laboratory offering the service must be licensed by CLIA for high-complexity testing.

Note: Separate Medical Policies may apply to some specific genetic tests and panels not addressed in the criteria below. See the Genetic Testing Section of the Medical Policy Manual Table of Contents for additional genetic testing policies.
This policy was developed based on the 2016 World Health Organization classification (WHO) of myeloid neoplasms and acute leukemia and applicable National Comprehensive Cancer Network clinical practice guidelines.

WORLD HEALTH ORGANIZATION (WHO)

WHO states that the presence of a SETBP1 mutation may aid in difficult to diagnose cases of chronic myelomonocytic leukemia (CMML) and atypical chronic myeloid leukemia (aCML).[2] WHO diagnostic criteria for chronic neutrophilic leukemia includes presence of CSF3R T618I or other activating CSF3R pathogenic variant. Furthermore, WHO criteria for essential thrombocytemia, prefibrotic/early primary myelofibrosis (prePMF), overt PMF, CMML, aCML, and MDS/MPN with ring sideroblasts and thrombocytosis include JAK2, MPL, and CALR mutation presence or absence in the diagnosis. A number of genes included in panels that are offered for these conditions do not have clear clinical utility and are not mentioned in the WHO classification, including GNAS, GNB1, and SUZ12.

NATIONAL COMPREHENSIVE CANCER NETWORK (NCCN)

Guidelines published by the National Comprehensive Cancer Network are also considered when genetic testing panels are reviewed for inclusion in this policy. There is limited research regarding SETBP1 mutations, though studies have reported that the presence of a SETBP1 mutation is associated with disease progression in myelodysplastic syndromes (MDS).[3] NCCN guidelines for myelodysplastic syndromes (MDS) include SETBP1 in a list of genetic variants providing presumptive evidence of MDS.

SUMMARY

Numerous genetic mutations are associated with various hematolymphoid neoplasms or disorders. Genetic panel tests may be used to evaluate several genes at the same time. The MPN Molecular Profile from Genoptix and the Next-Generation Sequencing, Acute Myeloid Leukemia, 8-Gene Panel from the Mayo Clinic include genetic testing for genes that are all relevant to several blood and lymph related cancers and disorders. These disorders have overlapping clinical characteristics, and genetic testing may help to confirm a diagnosis and guide future treatment decisions. In addition, practice guidelines recommend genetic testing for various hematolymphoid neoplasms or disorders to confirm or establish a diagnosis. Therefore, genetic panel tests may be considered medically necessary when policy criteria are met.

There are many genes that have been suggested to have a link with hematolymphoid neoplasms or disorders, but for which the clinical utility of testing has not been established. The Myeloid Molecular Profile panel from Genoptix, the GeneTrails AML MDS Genotyping panel from Oregon Health and Science University, the Hematological Malignancy Mutation Panel from Baylor Genetics, and the Targeted Cancer Gene Panel from Tricore Reference Laboratories includes genetic testing for genes in this category. Therefore, these tests are considered investigational.
REFERENCES


CODES

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<th>Description</th>
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**Date of Origin:** November 2016