Regence

Medical Policy Manual

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

**Date of Origin:** November 2016

**Section:** Genetic Testing

**Last Reviewed Date:** November 2016

**Policy No:** 09

**Effective Date:** December 1, 2016

**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.

**Background**

Genetic Panel Testing

Numerous genetic mutations 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 mutation 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 mutations 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 mutations 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 mutations 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). 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.
Note: This policy addresses genetic testing panels 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.

The MPN Molecular Profile panel from Genoptix may be considered medically necessary.

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

CLINICAL PRACTICE GUIDELINES

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 mutation. Furthermore, WHO criteria for essential thrombocythemia, 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.

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 gene mutations 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 includes genetic mutation 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.

REFERENCES


CROSS REFERENCES

Genetic Testing in Myeloid Neoplasms and Leukemia, Genetic Testing, No. 59
Evaluating the Utility of Genetic Panels, Genetic Testing, No. 64

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