Genetic Testing for Known Familial Mutations

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Genetic Testing for Known Familial Mutations is addressed by this guideline.

Description

When genetic testing reveals the cause of an inherited disease in an affected family member, the genetic change is called a 'known familial mutation' (KFM). Relatives of the affected individual should generally have genetic testing that targets this disease-causing KFM rather than full sequencing of a gene or a multi-gene panel.

KFM testing is less expensive, less complex, and avoids finding variants of uncertain clinical significance (VUS) that have unclear medical management implications.

Presymptomatic or diagnostic testing for known familial mutations should only be offered when the variant is considered disease-causing, or classified as pathogenic or likely pathogenic per American College of Medical Genetics and Genomics (ACMG) variant classification guidelines.[1]

If there is a KFM in the family, testing for this mutation should be performed prior to any other genetic testing for the disease in an individual.[2,3]

Note:

This benefit/harm statement only applies to those jurisdictions that do not have Medicare guidance. Based upon the clinical policy, following EviCore's criteria for genetic testing for known familial mutations will ensure that testing will be available to those members most likely to benefit from a genetic diagnosis. For those not meeting criteria, it ensures alternate diagnostic/management strategies are considered. However, it is possible that some members who would benefit from the testing, but do not meet criteria, will not receive an immediate approval for testing.

Criteria

Requests for genetic testing for Known Familial Mutations (KFM) are reviewed using the following criteria.

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Criteria: General Coverage Guidance

- Pre and post-test genetic counseling by an appropriate provider (as deemed by the Health Plan policy), AND
- No previous genetic testing of the requested gene that would have included the KFM, AND
- Member is a 1st, 2nd, or 3rd degree biological relative of the family member with the KFM, AND
- KFM is disease-causing (classified as pathogenic or likely pathogenic), AND
- Diagnostic Testing in Symptomatic Individuals:
  - Member exhibits symptoms consistent with the disease caused by the KFM, OR
- Presymptomatic or Predictive Testing in Asymptomatic Adults:
  - Member is 18 years of age or older, AND
- Healthcare providers can use the test results to provide significantly better medical care for the individual, AND
- Rendering laboratory is a qualified provider of service per the Health Plan policy.

Limits:

- Diagnostic or presymptomatic/predictive KFM testing will be allowed once per lifetime per condition.

Note:

For medical necessity criteria for presymptomatic/predictive testing of a known familial mutation in individuals younger than 18 years, see the guideline: *Genetic Testing to Predict Disease Risk*.

Billing and Reimbursement Considerations

- Once the mutation(s) that cause disease in the family have been identified, KFM testing is generally the only testing needed for that particular gene. As a result, if broad gene testing (for example, full gene sequencing or deletion/duplication analysis) is requested and a KFM has been identified in a family member, testing will be redirected to KFM testing.
- In rare circumstances, additional gene testing may be indicated following KFM testing, which will be assessed on a case-by-case basis.
- CPT codes specific for KFM testing (generally including language such as “known familial variant” in the code description) may not be used to bill for any other types of testing. There must be a documented KFM in the family. For example, the use of a KFM CPT code when billing part of a panel of genes, which is generally used as the initial step in identifying a disease-causing mutation in an individual, is not a correct use of these codes and is therefore not eligible for reimbursement.

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Criteria: Test-specific Guidelines

Test-specific guidelines are available for some tests designed to assess known familial mutations. For tests without a specific guideline, use the General Coverage Guidance above.

References

This guideline cites the following references.

1. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015; 17(5):405-24. doi: 10.1038/gim.2015.30.
2. U.S. Preventative Services Task Force. Final recommendation Statement BRCA-Related Cancer: Risk Assessment, Genetic Counseling, and Genetic Testing. August 20, 2019. Available at: https://www.uspreventiveservicestaskforce.org/uspstf/document/RecommendationStatementFinal/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing
3. Gupta A, Weiss JM, Axell L, et al. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2023 – October 30, 2023. Genetic/Familial High-Risk Assessment: Colorectal, available at: **https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal V2.2023 – October 30, 2023. ©2024 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines®, go online to **NCCN.org** .