Testing and Services Overview

Quest Vantage™
Cancer Testing Solutions

Quest Vantage offers a portfolio of hereditary cancer tests and services. It gives practices the flexibility of multiple test options for focused or comprehensive risk testing, a lab that's simple to work with, and expert-guided education tools for both practitioner and patient. The value to you: improved actionability, efficiency, and patient engagement. Because a test result is only as good as the action it inspires.

Quest Vantage Test Offering (available single genes on back)*	Code
BRCAvantage® Ashkenazi Jewish Screen Common founder mutations *BRCA1* c.68_69delAG, *BRCA1* c.5266dupC, *BRCA2* c.5946delT	91864
BRCAvantage® Ashkenazi Jewish Screen with Reflex to BRCAvantage®, Comprehensive Ashkenazi Jewish screen; if negative reflex to BRCAvantage Comprehensive	92140
BRCAvantage® Comprehensive *BRCA1, BRCA2*	91863
GIvantage™ Hereditary Colon Cancer Panel *APC, BMPR1A, CDH1, EPCAM, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, SMAD4, STK11, TP53*	93791
Juvenile Polyposis Panel *BMPR1A* and *SMAD4*	94053
Lynch Syndrome Panel *MLH1, MSH2 (including EPCAM), MSH6, PMS2*	91461
MYvantage™ Hereditary Comprehensive Cancer Panel *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A* (p14 and p16), *CHEK2, EPCAM, MEN1, MLH1, MSH2, MSH6, MUTYH, NBN, NF1, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, RET, SDHB, SDHC, SDHD, SMAD4, STK11, TP53, VHL*	93768
MYvantage™ Single Site Specific mutation testing for a known familial mutation. Records documenting the mutation must be provided	93945

* For the complete test offering or menu go to QuestVantage.com. For additional testing information, please call 1.866.GENE.INFO.

Ordering and Reporting

Ordering and reporting can be done by paper or electronically, using Care360® or other EMR interfaces. Required sample volume is 2–5mL. Specimens can be collected with a collection kit using standard 4mL tubes, or at one of our more than 2,000 Patient Service Centers. Samples can be picked up by a Quest Diagnostics courier or, when courier service is not available, by FedEx with a prepaid mailer.

Turnaround Time

Two to three weeks on average upon receipt of sample in the laboratory for each Quest Vantage test if the family history form and order are complete, patient meets criteria, and health plan does not require preauthorization. TAT may vary based on some insurance authorizations or on delays caused by incomplete orders.

Health Plan Coverage

We are in-network with most national plans and many local plans.

Quest Diagnostics™

Concierge Service

Our team is committed to helping you and your patients navigate the complexities of insurance reimbursement.

- **Insurance verification**
  Our team will verify coverage and obtain preauthorization as required by your patient's health plan. This is done upon receipt of completed paperwork. The insurance verification may be done with or without receipt of a patient specimen. We will manage this process from beginning to end.
- **Estimated patient responsibility**
  If your patient's out-of-pocket expense is estimated to be over $350, we will notify you and/or your patient prior to performing the test.

Financial Assistance

We provide an easy-to-use financial assistance program that limits out-of-pocket expenses to $200 for qualified patients with income at or below 400% of the federal poverty level for qualified tests. For uninsured and underinsured patients who meet or fall below the federal poverty level, qualified tests may be provided at no charge. For patients who require additional financial assistance, Quest Diagnostics offers payment plans of 0% financing for a 12-month period. Visit QuestVantage.com for more details.

Technical Specifications

Next-generation sequencing (NGS) on the Illumina NextSeq 500 platform, with alignment using our proprietary software, with confirmation as needed by array CGH for assessing deletions and duplications suspected by NGS.

Technology and Design

- Next-generation sequencing method that interrogates all coding regions and splice junctions to detect sequence variations, deletions and duplications in the genes. Certain deep intronic regions are queried for known pathogenic variants
- Random shearing of DNA is followed by bait tile capture of target sequences. This strategy creates unique clones and an enriched population of target sequences. Our methodology significantly reduces potential errors caused by Sanger sequencing and PCR-based methods, such as allele dropout, oversampling of an individual clone and polymorphisms occurring under the PCR primer
- Alignment using proprietary software in combination with the Illumina NextSeq 500 platform enables extremely accurate allele identification
- Deletion and duplication are assessed by bioinformatic analysis of sequencing reads and confirmed as necessary by a custom targeted microarray

Analytic Sensitivity and Specificity

- >99.9% sensitivity and specificity in the validation study

Base Pair Coverage

- Our quality metric requires each base of every exon to be sequenced from at least 20 different clones. With this stringent quality metric, there has not been a false positive or false negative result in our validation series

Variant Classification

Classification Methods

- Variant classification using the American College of Medical Genetics (ACMG) 5-tier classification system
- Initial variant assessment performed by a team of scientists with expertise in variant analysis
- Content acquisition consisting of both public and private biomedical databases and peer-reviewed journals
- Integration of data from published literature and public mutation databases, including BRCAShare and in silico prediction tools, as well as what is known about evolutionary conservation of certain amino acids of a particular gene into a framework for organizing and describing biological evidence that includes patient phenotypes, disease mechanisms, and cellular and molecular mechanisms
- The final interpretation is performed by board-certified directors at Quest Diagnostics Nichols Institute and multiple reviews are performed for every positive and variant of unknown significance (VUS) case
- When a VUS is identified, the relatives of the affected family member may qualify for a family study program at no cost

Reclassification

- Reclassified variants will be communicated to the ordering provider

Genetic Counseling

Our team of genetic counselors is available from 8:30am to 8:00pm EST by calling Quest Genomics Client Services at **1.866.GENE.INFO** (1.866.436.3463) to help medical professionals with genetics-related questions, including appropriate test selection and interpretation of results. We also connect patients with external genetic counselors as requested and when required by health plan before or after testing has been ordered.

Single Gene Test Codes

(Single Gene - Test Code) *APC – 93797, CDH1 – 92568, CDKN2A – 93939, CHEK2 – 93940, MEN1 – 93942, MLH1 – 91460, MSH2 with EPCAM – 91471, MSH6 – 91458, MUTYH – 93944, NF1 – 93941, PALB2 – 92571, PMS2 – 91457, PTEN – 92566, RET – 93796, STK11 – 92565, TP53 – 92560, VHL – 93943*

Quest Diagnostics™