Medica Coverage Policy

Policy Name: Genetic and Pharmacogenetic Testing
Effective Date: 12/17/2018

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for specific coverage information. If there is a difference between this general information and the member’s plan document, the member’s plan document will be used to determine coverage. With respect to Medicare, Medicaid and MinnesotaCare members, this policy will apply unless these programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Medica coverage policy may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care and treatment.

This policy addresses the following four types of testing:

I. Genetic testing for diagnosis and prediction of risk of heritable diseases
II. Carrier testing for heritable diseases
III. Molecular and genomic pathology testing
IV. Pharmacogenetic testing for drug metabolism

Medica has a number of disease- and/or condition-specific criteria for genetic testing, outlined in related coverage and utilization management policies. Please refer to Attachment 1 at the end of this document for a list of those policies. If a separate policy does not exist, the following criteria apply.

**Single Gene Testing for Heritable Diseases**

The following single gene tests ARE COVERED.

<table>
<thead>
<tr>
<th>Single Gene Test</th>
<th>Heritable Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-1 antitrypsin disease (SERPINA1)</td>
<td>Huntington's disease (HTT, HD (Huntington))</td>
</tr>
<tr>
<td>Alpha thalassemia (HBA1/HBA2)</td>
<td>Maple syrup urine disease (BCKDHA, BCKDHB, DBT)</td>
</tr>
<tr>
<td>Beta thalassemia</td>
<td>Marfan’s syndrome (TGFBR1, TGFBR2)</td>
</tr>
<tr>
<td>Bloom syndrome (BLM)</td>
<td>Mucolipidosis type IV (MCOLN1, mucolipin 1)</td>
</tr>
<tr>
<td>Canavan disease (ASPA (aspartoacylase A))</td>
<td>Muscular dystrophy (DMD (dystrophin))</td>
</tr>
<tr>
<td>Charcot Marie Tooth (PMP-22)</td>
<td>Neimann-Pick disease, type A (SMPD1, sphingomyelin phosphodiesterase)</td>
</tr>
<tr>
<td>Congenital adrenal hyperplasia/21 hydroxylase deficiency (CYP21A2)</td>
<td>Nonsyndromic hearing loss (GJB2, GJB6)</td>
</tr>
<tr>
<td>Cystic fibrosis (CFTR)</td>
<td>Phenylketonuria (PAH)</td>
</tr>
<tr>
<td>Factor V Leiden (F5 (Factor V))</td>
<td>Prader-Willi-Angelman syndrome (SNRPN, GABRA5, NIPA1, UBE3A, ANCR, GABRA)</td>
</tr>
<tr>
<td>Familial dysautonomia (IKBKAP)</td>
<td>Rett syndrome (FOXP1, MECP2)</td>
</tr>
<tr>
<td>Fanconi anemia (FANCC, FANCD)</td>
<td>Sickle cell disease (HBB Gene)</td>
</tr>
<tr>
<td>Fragile X syndrome (FMR1)</td>
<td>Spinal muscular atrophy (SMN1)</td>
</tr>
</tbody>
</table>
Medica Coverage Policy

I. Single gene and multi-gene panel testing for **diagnosis and/or prediction of risk for heritable diseases not listed above** is COVERED when documentation in the medical record indicates that the member meets either **A** or **B** below:
   (NOTE: For all other genetic testing, the following criteria apply when no specific policy exists. Please refer to Attachment 1 at the end of this document for a list of those policies).
   **A.** The test is **ordered** by a board-certified medical geneticist or genetic counselor not employed by or contracted with the commercial laboratory performing the testing and medical records document a detailed family history/pedigree and pre-test genetic counseling.
   **B.** For tests **ordered** by other than a geneticist or genetic counselor all of the following criteria must be met:
      1. Medical records document a detailed family history/pedigree and **pre-test** genetic counseling by **one of the following**:
         a. A board-certified medical geneticist not employed or contracted with the commercial laboratory performing the testing.
         b. A board-certified genetic counselor not employed or contracted with the commercial laboratory performing the testing.
         c. A board-certified Genetic Clinical Nurse or Advanced Practice Nurse in Genetics (APNG) not employed or contracted with the commercial laboratory performing the testing.
         d. Other qualified healthcare professional with specialized education and training in medical genetics not employed or contracted with the commercial laboratory performing the testing.
      2. The member has **one of the following**:
         a. Current signs and/or symptoms suggesting a genetic disease
         b. Family history indicating that the member is at high risk for a genetic disease.
      3. Medical records document how the test(s) will lead to changes in treatment decisions (e.g., initiate a new course of therapy, alter existing therapy, determine/change level of surveillance, or make reproductive decisions) and/or health outcome for the member being tested.

II. Single gene testing for **carrier status of heritable diseases** IS COVERED when documentation in the medical records indicates that the member meets either **A** or **B** below:
   (NOTE: The following criteria apply when no specific policy exists. Please refer to Attachment 1 at the end of this document for a list of those policies).
   **A.** The test is ordered by a board-certified medical geneticist or genetic counselor not employed by or contracted with the commercial laboratory performing the testing and medical records document a detailed family history/pedigree and pre-test genetic counseling.
   **B.** For tests **ordered** by other than a geneticist or genetic counselor all of the following criteria must be met:
      1. Medical records document a detailed family history/pedigree and **pre-test** genetic counseling by **one of the following**:
         a. A board-certified medical geneticist not employed by or contracted with the commercial laboratory performing the testing.
         b. A board-certified genetic counselor not employed by or contracted with the commercial laboratory performing the testing.
         c. A certified Genetic Clinical Nurse or Advanced Practice Nurse in Genetics (APNG) not employed by or contracted with the commercial laboratory performing the testing.
         d. Other qualified healthcare professional with specialized education and training in medical genetics not employed by or contracted with the commercial laboratory performing the testing.
      2. The member is currently pregnant or contemplating pregnancy and is at high risk of being a carrier of a specific genetic disorder based on family history. **Examples include, but are not limited to:**
         a. One parent is a known carrier of a clinically significant X-linked recessive, or autosomal recessive disease (e.g., hemophilia, cystic fibrosis, Duchenne muscular dystrophy, sickle cell anemia, or Tay Sachs disease).
         b. A child of the member(s) has been identified with an autosomal recessive or X-linked disorder.
         c. One or both parents have a first or second degree relative who is affected by a specific genetic disorder or the
first-degree relative has an affected child with an autosomal recessive or X-linked disorder.

d. There is a maternal history of two or more fetal losses.

3. The test results will affect reproductive choices.

NOTE: Multigene panel testing for carrier status is addressed in the following Medica Coverage Policy: Expanded Carrier Testing for Genetic Diseases in Adults.

III. Single and multigene molecular and genomic pathology testing for cancer management IS COVERED when documentation in the medical record indicates that the member meets all of the following criteria:

A. The test is ordered by a board-certified pathologist, geneticist, or oncologist/hematologist not employed by or contracted with the commercial laboratory performing the testing.

B. Medical records document how the test(s) will lead to increased precision in diagnosis and treatment.

IV. Pharmacogenetic testing for drug metabolism

A. Pharmacogenetic testing IS COVERED when testing for a specific gene biomarker is required by the U.S. Food and Drug Administration (FDA) prior to initiating therapy with a drug as noted in the section heading “Indications and Usage” of the FDA-approved prescribing label. Refer to Attachment 2 at the end of this document for a list of these tests.

B. Pharmacogenetic testing for all other indications IS COVERED when documentation in the medical record indicates that all of the following criteria are met:
1. The member is a candidate for a targeted drug therapy associated with a specific gene biomarker or gene mutation.
2. There is reliable evidence that a specific genetic biomarker or mutation is directly linked to a specific therapeutic drug target.
3. Medical records document how the test results will lead to changes in treatment decisions and/or health outcome for the member being tested.

Other Considerations

1. Chromosome analysis, including karyotyping and g-banding, is covered.

2. Most tests, particularly those for inherited disorders, should be accompanied by pre and post-test patient counseling by a board certified genetic counselor, medical geneticist, genetic nurse or other qualified healthcare professional not employed by or contracted with the commercial laboratory performing the testing. Genetic professionals are not excluded if they are employed by or contracted with a laboratory that is part of a health care system that routinely delivers health care services beyond just the laboratory test.

3. All testing requires an order by a licensed healthcare professional not employed by or contracted with the commercial laboratory performing the testing.

4. All testing must be FDA approved or performed in a laboratory licensed under CLIA for high-complexity testing. CLIA standards cover how tests are performed, the qualifications of laboratory personnel, and quality control and testing procedures for each laboratory. By controlling the quality of laboratory practices, CLIA standards are designed to ensure the analytical validity of genetic tests.

5. Generally, it is not necessary to repeat genetic testing for a heritable disease. However, as science evolves, genetic test results will likely require re-interpretation by a medical geneticist or genetic counselor. The rare examples in which repeat testing may be necessary include the use of inaccurate methodology with previous testing or discovery of a new mutation relevant to a disease.

Genetic testing is excluded and therefore NOT COVERED when:

1. The test is performed in the absence of symptoms or high risk factors for a genetic disease.

2. Knowledge of genetic status will not affect treatment decisions, surveillance, reproductive decisions and/or health outcome of the member being tested.

3. The test is obtained without an order from a licensed healthcare professional, including direct-to-consumer testing (mail order,
online ordering).
4. The test is performed as a general screening tool, other than newborn screening performed in accordance with state mandates.
5. The testing is performed to screen for nonmedical traits (e.g., eye color, hair color).
6. The testing is performed solely to determine the sex of a child.
7. The testing is performed solely to determine the paternity of a child.

**Description**

Genetic tests are laboratory tests performed on a sample of blood, saliva, hair, skin, or other tissue that identify changes in chromosomes, genes, or proteins. The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person’s chance of developing or passing on a genetic disorder. The human genome is believed to contain approximately 20,000 genes. Of these, over 4,000 are thought to cause disease. Genetic testing utilizes biochemical assays, direct examination of genetic material, or examination of chromosomes or genetic markers to:

1. Confirm a diagnosis when a member has signs or symptoms that suggest a genetic disease (diagnostic testing)
2. Estimate the likelihood of a member developing a genetic disease (predictive testing)
3. Identify which family members are at risk for a certain genetic condition already known to be present in their family (presymptomatic testing)
4. Determine the likelihood of cancer recurrence (prognostic testing)
5. Determine if a member has one copy of a gene that, if passed along to a child, may result in a genetic disorder in the child (carrier testing)
6. Determine a member's response to drugs and susceptibility to drug-induced adverse effects (pharmacogenetic testing)
7. Determine whether an embryo (preimplantation testing) or developing fetus has a genetic mutation (prenatal testing)
8. Identify disorders in newborns that might have long-term health effects (newborn screening)
9. Identify a member for legal reasons (forensic testing)
10. Learn more about the contributions of genes to health and disease (research testing).

Genetic variants, also known as mutations, are changes in the genetic code. Variants are classified as benign, disease-causing (pathogenic) or of uncertain significance based on how likely they are to change the way a gene works. Another possible outcome of genetic testing is that no genetic alteration is found. However, this does not necessarily mean that the member does not have a variant, only that one was not detected. Furthermore, the absence of known variants does not mean there is no risk of disease, especially with regard to conditions for which not all of the disease-causing genes have been identified.

Historically, genetic testing has been done one gene at a time. With the advent of new technology, such as next generation sequencing (NGS) and chromosomal microarray, scientists can now examine many genes simultaneously. As a result, a number of genetic testing panels have been developed and introduced in the areas of cancer, cardiovascular disease, neurologic disease, psychiatric disorders, and reproductive testing. NGS multigene panels are appealing for their potential to reduce costs and improve efficiency by decreasing the time involved, the number of patient visits and the number of test samples required and are being used clinically for a number of conditions.

However, despite its integration into more areas of clinical medicine, the use of multigene panels is not without its limitations. First, testing many genes does not always mean better information. Multigene panels do not include every possible gene that could be related to a member’s medical condition. Conversely, panels often include genes that have only a low to moderate risk of causing medical problems, genes that are not well understood or clinically actionable, or genes that are not relevant to the reason for testing, but may have clinical implications for the member being tested. Another issue with multigene panel testing is the variability among panels and processes themselves. The vast majority of panels are laboratory developed tests (LDTs) that are proprietary to the lab doing the testing. Each lab may use different sequencing equipment, different testing processes, as well as different databases and computational systems for identifying genetic variants. Therefore, a multigene panel should be carefully selected by a genetics professional based on the member’s medical and family history.

Pharmacogenetics, also known as pharmacogenomics, is a type of genetic testing that attempts to use personal gene-based information to determine the proper drug and dosage for a member. Pharmacogenetic testing seeks to determine how a drug is absorbed, metabolized or cleared from the body of a member based on their genetic makeup. Test results are intended to allow the clinician to predict the patient’s response to pharmacotherapy, assist in making treatment choices, personalize drug dosages in order to maintain a
consistent drug level in the body, and avoid adverse reactions from overdose or suboptimal effects from under medication. However, tailoring drug therapy based on genetic variations has a number of limitations, including the presence of multiple genes affecting a particular drug response and distribution, non-genetic factors affecting response, and unclear clinical benefits associated with testing. Despite this, many pharmacogenetic tests are currently available.

**FDA Approval**
Devices and commercially marketed genetic testing kits are subject to FDA approval. Individual genetic testing laboratories are subject to the regulatory standards of the Clinical Laboratory Improvement Act (CLIA) of 1988.

**Prior Authorization**
Prior authorization is required for testing outlined in the Utilization Management Policies outlined in Attachment 1. Additionally, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

**Coding Considerations**
Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

Original Effective Date: 12/1/2007

Re-Review Date(s):
10/21/2009
10/29/2011
2/19/2014
3/18/2015
11/16/2016
9/19/2018
Attachment 1: Gene/Condition Specific Policies

The following lists are subject to change without notice. Consult www.medica.com / Providers / Medical Policies for a complete listing or Medica's Coverage and Utilization Management Policies.

Medica has the following Coverage Policies related to genetic tests:
1. Apolipoprotein E (APOE) Genetic Testing for Prediction and Management of Cardiovascular Disease
2. Bladder Cancer Screening, Diagnosis and Monitoring Using Ancillary Urinary Tests
3. Liquid Biopsy: Testing of Circulating Tumor Cells or Cell-Free Tumor DNA/Cytochrome P450 (CYP450) Variant Genotyping (e.g., CYP2D6, CYP2C9, CYP2C19, CYP1A2, CYP3A4)
4. Expanded Carrier Testing for Genetic Diseases in Adults
5. Fecal/Stool DNA (sDNA) Testing for Colorectal Cancer Screening and Monitoring
6. Gene Expression Profiling Assays for Breast Cancer
7. Gene Expression Profiling Assays for Predicting Colon Cancer Recurrence Risk
8. Gene Expression Profiling for Assessing Cancers of Unknown Origin
9. Gene Expression Profiling for Detection of Heart Transplantation Rejection
10. Genetic Testing: ScoliScore™ TM Adolescent Idiopathic Scoliosis (AIS) Prognostic Test
12. Genetic Testing for Alzheimer Disease
13. Genetic Testing for Inherited Susceptibility to Malignant Melanoma
14. Genetic Testing for Prostate Cancer
15. Genetic Testing for Thyroid Cancer
16. Human Leukocyte Antigen-DQ (HLA-DQ) Genetic Testing for Diagnosis of Celiac Disease
17. KRAS Mutation Analysis for Predicting Response to Drug Therapy
18. Laboratory Tests
19. Methylene tetrahydrofolate Reductase (MTHFR) Gene Mutation Testing
20. Pharmacogenetic Testing of the VKORC1 Gene for Warfarin Response
21. Pharmacogenetic Testing to Predict Toxicity to 5-Fluorouracil (5-FU)/Capecitabine-Based Chemotherapy
23. VeriStrat Proteomic Testing
24. Whole Genome Testing

Medica has the following Utilization Management policies related to genetic tests:
1. Comparative Genomic Hybridization (CGH) Microarray Testing
2. Genetic Testing for Cardiac Channelopathies
3. Genetic Testing for Cardiomyopathies
4. Genetic Testing For Susceptibility to Hereditary Breast and Ovarian Cancer
5. Genetic Testing for Susceptibility to Colorectal Cancer (CRC) Syndromes
7. Whole Exome Sequencing
## Attachment 2: Pharmacogenetic Testing Required by FDA

The following list is subject to change without notice.

<table>
<thead>
<tr>
<th>Generic Drug Name</th>
<th>Brand Name</th>
<th>Condition</th>
<th>Gene/Protein Name</th>
<th>FDA Approved Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>azathioprine</td>
<td>Imuran</td>
<td>Transplant rejection, rheumatoid arthritis</td>
<td>Thiopurine S-methyltransferase (TPMT)</td>
<td>N/A</td>
</tr>
<tr>
<td>ceritinib</td>
<td>Zykadia</td>
<td>Non-small cell lung cancer (NSCLC)</td>
<td>Anaplastic lymphoma kinase (ALK)</td>
<td>• Vysis ALK Break Apart FISH Probe Kit (Abbott Molecular)</td>
</tr>
<tr>
<td>cobimetinib</td>
<td>Cotellic</td>
<td>Unresectable or metastatic melanoma</td>
<td>BRAF V600E or V600K</td>
<td>• cobas 4800 BRAF (Roche Molecular Systems, Inc) • THxID BRAF test (bioMérieux Inc)</td>
</tr>
<tr>
<td>crizotinib</td>
<td>Xalkori</td>
<td>Non-small cell lung cancer (NSCLC)</td>
<td>Anaplastic lymphoma kinase (ALK)</td>
<td>• Vysis ALK Break Apart FISH Probe Kit (Abbott Molecular) • ALK (D5F3) CDx Assay (Ventana Medical Systems)</td>
</tr>
<tr>
<td>dabrafenib</td>
<td>Tafinlar</td>
<td>Unresectable or metastatic melanoma</td>
<td>BRAF V600E and/or V600K</td>
<td>• THxID BRAF test (bioMérieux Inc)</td>
</tr>
<tr>
<td>eliglustat</td>
<td>Cerdelga</td>
<td>Gaucher disease type 1</td>
<td>CYP2D6</td>
<td>• xTAG CYP2D6 Kit v3 (Luminex Molecular Diagnostics, Inc.) • Roche AmpliChip CYP450 microarray (Roche Molecular Systems, Inc.)</td>
</tr>
<tr>
<td>erlotinib</td>
<td>Tarceva</td>
<td>Metastatic non-small cell lung cancer (NSCLC)</td>
<td>EGFR</td>
<td>• cobas EGFR Mutation Test v2 (Roche Molecular Systems, Inc.)</td>
</tr>
<tr>
<td>imatinib mesylate</td>
<td>Gleevec</td>
<td>Aggressive Systemic Mastocytosis (ASM)</td>
<td>KIT D816V</td>
<td>• KIT D816V Mutation Detection by PCR for Gleevec Eligibility in Aggressive Systemic Mastocytosis (ASM) (ARUP)</td>
</tr>
<tr>
<td>Generic Drug Name</td>
<td>Brand Name</td>
<td>Condition</td>
<td>Gene/Protein Name</td>
<td>FDA Approved Tests</td>
</tr>
<tr>
<td>-------------------</td>
<td>------------</td>
<td>-----------</td>
<td>-------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>imatinib mesylate</td>
<td>Gleevec</td>
<td>Myelodysplastic Syndrome/Myeloproliferative Disease (MDS/MPD)</td>
<td>PDGFRB gene rearrangement</td>
<td>• PDGFRB FISH for Gleevec Eligibility in Myelodysplastic Syndrome/Myeloproliferative Disease (MDS/MPD) (ARUP)</td>
</tr>
</tbody>
</table>
| ivacaftor         | Kalydeco   | Cystic Fibrosis | G551D mutation in CTFR gene | • Illumina MiSeqDx Cystic Fibrosis Clinical Sequencing Assay (Illumina, Inc)  
• Illumina MiSeqDx Cystic Fibrosis 139-Variant Assay (Illumina, Inc)  
• eSensor CF Genotyping Test (Osmetech Molecular Diagnostics)  
• xTAG Cystic Fibrosis 60 Kit v2 (Luminex Molecular Diagnostics Inc.)  
• xTAG Cystic Fibrosis 39 Kit v2 (Luminex Molecular Diagnostics Inc.)  
• InPlex CF Molecular Test (Third Wave Technology, Inc.)  
• Cystic Fibrosis Genotyping Assay (Celera Diagnostics)  
• Tag-It Cystic Fibrosis Kit™ (Bioscience Corporation) |
<p>| lumacaftor        | Orkambi    | Treatment of cystic fibrosis in patients age 12 and older | F508del in CFTR gene | • Same as number 7 (ivacaftor) above |
| olaparib capsules | Lynparza    | Advanced ovarian cancer associated with BRCA | | • BRACAnalysis CDx test (Myriad Genetics, Inc.) |</p>
<table>
<thead>
<tr>
<th>Generic Drug Name</th>
<th>Brand Name</th>
<th>Condition</th>
<th>Gene/Protein Name</th>
<th>FDA Approved Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>13. osimertinib</td>
<td>Tagrisso</td>
<td>Metastatic epidermal growth factor receptor (EGFR) T790M mutation-positive non-small cell lung cancer</td>
<td>EGFR T790M mutation</td>
<td>• cobas EGFR Mutation Test v2 (Roche Molecular Systems, Inc)</td>
</tr>
<tr>
<td>14. pembrolizumab</td>
<td>Keytruda</td>
<td>Metastatic non-small cell lung cancer (NSCLC) whose tumors express PD-L1 as determined by an FDA-approved test</td>
<td>Programmed death ligand 1 (PD-L1) expression</td>
<td>• PD-L1 IHC 22C3 pharmDx kit (Dako North America, Inc.)</td>
</tr>
<tr>
<td>15. tetrabenazine</td>
<td>Xenazine®</td>
<td>Treatment of Huntington’s Disease</td>
<td>CYP2D6</td>
<td>• xTAG CYP2D6 Kit v3 (Luminex Molecular Diagnostics, Inc.) • Roche AmpliChip CYP450 microarray (Roche Molecular Systems, Inc.)</td>
</tr>
<tr>
<td>16. trametinib</td>
<td>Mekinist</td>
<td>Unresectable or metastatic melanoma</td>
<td>BRAF V600E and/or V600K</td>
<td>• THxID BRAF test (bioMérieux Inc)</td>
</tr>
<tr>
<td>17. trastuzumab</td>
<td>Herceptin</td>
<td>Breast, central nervous system, advanced gastric, advanced esophageal and esophagogastric cancers</td>
<td>HER2</td>
<td>N/A – See Medica Drug Policy: Herceptin (trastuzumab)</td>
</tr>
<tr>
<td>18. vemurafenib</td>
<td>Zelboraf</td>
<td>Unresectable or metastatic melanoma</td>
<td>BRAF V600E</td>
<td>• cobas 4800 BRAF (Roche Molecular Systems, Inc)</td>
</tr>
<tr>
<td>19. venetoclax</td>
<td>Venclexa™</td>
<td>Chronic Lymphocytic Leukemia with 17p Deletion</td>
<td>TP53 (containing tumor protein p53 gene, located on chromosome 17p)</td>
<td>• Vysis CLL Fish Probe Kit (Abbott Molecular, Inc.)</td>
</tr>
</tbody>
</table>
Attachment 3: Glossary

1. An allele is an alternative form of a gene that is located at a specific position on a specific chromosome. Humans inherit one allele from their mother and another allele from their father. The physical characteristics (e.g., eye color, hair color, skin color) of a member depend on both of the alleles. If the alleles are different, the dominant allele will be expressed, while the effect of the other allele, called recessive, is masked. In the case of a recessive genetic disorder, a member must inherit two copies of the mutated allele in order for the disease to be present.

2. A chromosome is an organized package of DNA found in the nucleus of the cell. Humans have 23 pairs of chromosomes—22 pairs of numbered chromosomes, called autosomes, and one pair of sex chromosomes, X and Y. Each parent contributes one chromosome to each pair so that offspring get half of their chromosomes from their mother and half from their father.

3. Deoxyribonucleic acid (DNA) is the hereditary material in humans and almost all other organisms.

4. A gene is the basic physical and functional unit of heredity. Genes, which are made up of DNA, act as instructions to make molecules called proteins. Genes are passed from parents to offspring and contain the information needed to specify traits.

5. Heritable disorders are conditions that are caused by gene mutations which can be inherited (passed down from parent to child). These typically are life-long mutations that affect multiple family members.

6. Multigene panel testing is genetic testing that uses next-generation sequencing to test multiple genes simultaneously, and is also called multiple-gene panel testing and multiple-gene testing.

7. A mutation is a permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. Mutations are also referred to as variants.

8. Next-generation sequencing (NGS), also known as massively parallel or high through-put sequencing, is an automated method of sequencing DNA, that can process many genes at one time. NGS is used to test multiple genes simultaneously. This is known as multigene panel testing, also known as multiple-gene panel testing or multiple-gene testing. Using NGS, DNA sequencing is less costly and less time-consuming than traditional manual DNA sequencing of one gene at a time.

9. A variant, also known as a gene mutation, is a permanent alteration in the DNA sequence that makes up a gene, such that the sequence differs from what is found in most people. There are also variants known as benign DNA variants where the alteration in the DNA sequence does not cause a change in the function of the gene. Mutations can vary in size; they can affect a single DNA base pair or be due to small deletions or insertions or rearrangements of DNA base pairs. Larger duplication and/or deletions of varying sizes include segments of a chromosome that can include multiple genes.

10. X-linked is a trait located on the X chromosome. Humans and other mammals have two sex chromosomes, the X and the Y. In an X-linked or sex linked disease, it is usually males that are affected because they have a single copy of the X chromosome that carries the mutation. In females, the effect of the mutation may be masked by the second healthy copy of the X chromosome.