Blue Cross and Blue Shield of Nebraska is proud to work with our provider network to serve your patients, our members. We are updating several medical policies. Please review the changes and effective dates outlined here:

REVISED MEDICAL POLICIES FOR GENETIC TESTING

Medical Policy: V.59 Genetic Testing: Hereditary Cancer Susceptibility Syndrome
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

***APC* Sequencing and/or Deletion/Duplication Analysis**

I. *APC* sequencing and/or deletion/duplication analysis (81201, 81203) for familial adenomatous polyposis (FAP) is considered **medically necessary** when:
   A. The member has a history of any of the following:
      1. 20 or more cumulative adenomas, **OR**
      2. Multifocal/bilateral congenital hypertrophy of the retinal pigment epithelium (CHRPE).

II. *APC* sequencing and/or deletion/duplication analysis (81201, 81203) for familial adenomatous polyposis (FAP) is considered **investigational** for all other indications.

Medical Policy: V.60 Oncology: Molecular Analysis of Solid Tumors and Hematologic Malignancies
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

Tumor-Type Agnostic Solid Tumor Molecular Profiling Panel Tests with IHC and Cytogenetic Analyses

I. Tumor-type agnostic solid tumor molecular profiling panel tests with IHC and cytogenetic analyses (0211U, 81455, 0379U) are considered **medically necessary** when:
   A. The member has recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer, **AND**
   B. The member is seeking further cancer treatment (for example, therapeutic chemotherapy).

II. Repeat testing via a tumor-type agnostic solid tumor molecular profiling panel with IHC and cytogenetic analyses (0211U, 81455, 0379U) is considered **medically necessary** when:
   A. The member has progression of any of the following:
      1. Metastatic colon cancer, **OR**
      2. Advanced or metastatic non-small cell lung cancer (NSCLC), **OR**
      3. Advanced or metastatic gastric adenocarcinoma, **OR**
      4. Metastatic prostate cancer, **OR**
      5. Ovarian cancer that is platinum sensitive.

III. Tumor-type agnostic molecular profiling panel tests with IHC and cytogenetic analyses (0211U, 81455, 0379U) are considered **investigational** for all other indications.

Tumor Specific *ESR1* Variant Analysis

I. Tumor specific *ESR1* variant analysis (81479) in solid tumors is considered **medically necessary** when:
   A. The member is a postmenopausal female or adult male with the following:
      1. ER-positive and HER2-negative breast cancer, **AND**
      2. Disease progression after one or two prior lines of endocrine therapy, including one line containing a CDK4/6 inhibitor.

Medical Policy: V.61 Oncology: Circulating Tumor DNA and Circulating Tumor Cells (Liquid Biopsy)
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

Colorectal Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)

I. Colorectal cancer focused panel tests via circulating tumor DNA (ctDNA) (81210, 81275, 81311, 81403, 81479) are considered **medically necessary** when:
   A. Member has metastatic colorectal adenocarcinoma, **AND**
   B. Panel includes *KRAS, NRAS,* and *BRAF* analysis, **AND**
   C. At least one of the following:
      1. The member is medically unfit for invasive tissue sampling (biopsy), **OR**
      2. Biopsy was performed, but material was insufficient for molecular analysis, **OR**
      3. Biopsy was performed, but molecular analysis was not able to be completely assessed on tissue due to availability of testing methodologies.

II. Colorectal cancer focused panel tests via circulating tumor DNA (ctDNA) (81210, 81275, 81311, 81403, 81479) are considered **investigational** for all other indications.

Medical Policy: V.62 Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

***FMR1* Repeat and Methylation Analysis**

I. *FMR1* repeat and methylation analysis (81243, 81244) to establish or confirm a genetic diagnosis of Fragile X syndrome or Fragile X-associated disorders is considered **medically necessary** when:
   A. The member has unexplained intellectual disability or developmental delay, **OR**
   B. The member is male and has unexplained autism spectrum disorder, **OR**
   C. The member is female, **AND**
      1. One of the following:
         a. Phenotype compatible with Fragile X syndrome (examples: ADHD and/or other behavioral differences, typical facies [long face, prominent forehead, large ears, prominent jaw], mitral valve prolapse, aortic root dilatation), **OR**
         b. At least one close relative with an X-linked neurodevelopmental disorder, premature ovarian failure, ataxia or tremor, **OR**
   D. The member has primary ovarian insufficiency (cessation of menses before age 40), **OR**

E. The member is 50 years of age or older with progressive intention tremor and cerebellar ataxia of unknown origin.

II. *FMR1* repeat and methylation analysis (81243, 81244) to establish or confirm a genetic diagnosis of Fragile X syndrome or Fragile X-associated disorders is considered **investigational** for all other indications.

Medical Policy: V.65 Genetic Testing: Epilepsy, Neurodegenerative and Neuromuscular Disorders
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

Limb-Girdle Muscular Dystrophy Multigene Panel

I. Multigene panel analysis to establish a diagnosis of limb-girdle muscular dystrophy (81405, 81406, 81408, 81479) is considered **medically necessary** when:

A. The member displays slowly progressive, symmetrical weakness with any of the following clinical features of limb-girdle muscular dystrophy:
1. Limb-girdle pattern of weakness affecting proximal muscles of the arms and legs, **OR**
2. Scapuloperoneal weakness, **OR**
3. Distal weakness, **OR**
4. Elevated serum creatine kinase s, **OR**

B. The member is asymptomatic, **AND**
C. The member has a close relative diagnosed with limb-girdle muscular dystrophy whose genetic status is unavailable.

II. Multigene panel analysis to establish a diagnosis of limb-girdle muscular dystrophy (405, 81406, 81408, 81479) is considered **investigational** for all other indications.

Medical Policy: V.66 Genetic Testing: Cardiac Disorders
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

Hypertrophic Cardiomyopathy Panels

I. Genetic testing for hypertrophic cardiomyopathy via a multigene panel (81405, 81406, 81407, 81439) is considered **medically necessary** when:
A. The member has unexplained left ventricular hypertrophy (LVH), **AND**
1. Myocardial wall thickness of 15mm or greater (in adults), or a z-score of 3 or greater (in children) based on echocardiogram or cardiac MRI, **OR**
B. The member has a first-degree relative with sudden unexplained cardiac death (SUDS) and autopsy revealed an HCM phenotype.

II. Genetic testing for hypertrophic cardiomyopathy via a multigene panel (81405, 81406, 81407, 81439) is considered **investigational** for all other indications.

Medical Policy: V.67 Genetic testing: Gastroenterology Disorders (Non-Cancerous)

Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

***HLA-DQ* Genotyping Analysis**

I. *HLA-DQ2* and *HLA-DQ8* variant analysis (81370, 81375, 81376, 81377, 81382, 81383) to rule out celiac disease is considered **medically necessary** when:
   A. The member meets one of the following:
      a) The member has equivocal small-bowel histological finding in seronegative patients, **OR**
      b) The member is on a gluten-free diet AND in whom no testing for CD was done before gluten-free diet, **OR**
      c) The member has discrepant celiac-specific serology and histology, **OR**
      d) Patients with suspicion of refractory CD where the original diagnosis of celiac remains in question.

II. *HLA-DQ2* and *HLA-DQ8* variant analysis (81370, 81375, 81376, 81377, 81382, 81383) to rule out celiac disease is considered **investigational** for all other indications.

***HFE* Sequencing and/or Deletion/Duplication Analysis**

I. *HFE* sequencing and/or deletion/duplication analysis (81256, 81479) to establish a diagnosis of hereditary hemochromatosis is considered **medically necessary** when:
   A. The member has abnormal serum iron indices, especially elevated serum transferrin-iron saturation and/or elevated serum ferritin concentration, indicating iron overload, **OR**
   B. The member has a first-degree relative with a diagnosis of hereditary hemochromatosis, especially if the relative has Type I HH where the relative has two C282Y mutations (homozygous).

II. *HFE* sequencing and/or deletion/duplication analysis (81256, 81479) to screen for hereditary hemochromatosis in the general population is considered **investigational**.

III. *HFE* sequencing and/or deletion/duplication analysis (81256, 81479) to establish a diagnosis of hereditary hemochromatosis is considered **investigational** for all other indications.

Medical Policy: V.68 Genetic Testing: Metabolic, Endocrine, and Mitochrondrial Disorders
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

Maturity-Onset Diabetes of the Young Panel

I. Multigene panel analysis to establish or confirm a diagnosis of maturity-onset diabetes of the young (MODY) (81403, 81405, 81406, 81407, 81479) is considered **medically necessary** when:

   A. The member meets one of the following:

      1. The member has a diagnosis of diabetes within the first 6 months of life, **OR**
      2. The member has a diagnosis of diabetes before 35 years of age, **AND**

   B. The member meets one of the following:
      1. The member has features atypical for type 1 diabetes mellitus, including at least one of the following:

a) Absence of pancreatic islet autoantibodies, **OR**
b) Evidence of endogenous insulin production beyond the honeymoon period (i.e., 3-5 years after the onset of diabetes), **OR**
c) Measurable C-peptide in the presence of hyperglycemia (C-peptide 0.60 ng/mL or greater, or 0.2 nmol/L), **OR**
d) Low insulin requirement for treatment (i.e., less than 0.5 U/kg/d), **OR**
e) Lack of ketoacidosis when insulin is omitted from treatment, **OR**

2. The member has features atypical for type 2 diabetes mellitus, including at least one the following:

a) Onset of diabetes before age 45 years, **OR**
b) Lack of significant obesity, **OR**
c) Lack of acanthosis nigricans, **OR**
d) Normal triglyceride levels and/or normal or elevated high-density lipoprotein cholesterol (HDL-C), **AND**

C. The member has a family history of diabetes consistent with autosomal dominant inheritance **AND**
D. The panel includes, at a minimum, the following genes: *GCK*, *HNF1A*, and *HNF4A*.

II. Multigene panel analysis to establish or confirm a diagnosis of maturity-onset diabetes of the young (MODY) (81403, 81404, 81405, 81406, 81407, 81479) is considered **investigational** for all other indications.

Medical Policy: V.72 Genetic Testing Immune, Autoimmune, and Rheumatoid Disease
Effective: 07/01/2023
Preauthorization Required: Yes
Policy Statement:

Known Familial Variant Analysis for Immune, Autoimmune, and Rheumatoid Disorders

I. Targeted mutation analysis for a known familial variant (81403) for an immune, autoimmune, and rheumatoid disorder is considered **medically necessary** when:

A. The member has a close relative with a known pathogenic or likely pathogenic variant causing the condition.

II. Targeted mutation analysis for a known familial variant (81403) for an immune, autoimmune, and rheumatoid disorder is considered **investigational** for all other indications.