Effective for dates of service on and after March 23, 2025, the following updates will apply to the Carelon Medical Benefits Management, Inc. Clinical Appropriateness Guidelines. As part of the Carelon guideline annual review process, these updates are focused on advancing efforts to drive clinically appropriate, safe, and affordable health care services.

Genetic Testing

Carrier Screening in the Reproductive Setting

- **Standard carrier screening**: Removed CBC from the list of acceptable prior testing restrictions for hemoglobinopathy screening.
- **Expanded Carrier screening**:
    - Clarified that medical records should attest to adoption or consanguinity.
    - Expansive criteria to allow for multigene panels to include conditions with less than 1 in 100 carrier frequencies for individuals in a consanguineous partnership.
    - Removed requirement that alternate biochemical tests are not available, have provided an indeterminate result, or are less accurate than genetic testing.

Genetic Testing for Inherited Conditions

- Added expansive criteria to allow confirmatory genetic testing for individuals identified to have a pathogenic or likely pathogenic germline variant in genes with established clinical utility based on results of IRB approved clinical research studies.
- **Cardiac conditions**:
    - Expanded genetic testing criteria for hereditary cardiomyopathy syndromes in the pediatric population.
    - Added new expansive medical necessity criteria for hereditary aortopathies.
- **Neurological conditions**: Expanded criteria to allow SOD1 genetic testing in individuals with amyotrophic lateral sclerosis (ALS) when determined to be a candidate for FDA approved Qalsody (tofersen) treatment.
- **Thrombophilia testing**:
    - Removed restriction of low bleeding risk in individuals with an unprovoked VTE who are planning to stop anticoagulation.
    - Removed criterion (last bullet) to allow F5 and F2 genetic testing for individuals contemplating estrogen use when they have a first-degree relative with VTE and a known hereditary thrombophilia per ASH guidance.

Hereditary Cancer Testing

- Removed requirement that alternate biochemical tests are not available, have provided an indeterminate result, or are less accurate than genetic testing.

- Listed specific examples of somatic test findings that, per ASCO guideline, should generate consideration of germline testing (clarification).
- Expanded criteria to allow confirmatory genetic testing for individuals identified to have a pathogenic or likely pathogenic germline variant in genes with established clinical utility based on results from direct-to-consumer genetic testing or results from an IRB approved clinical research study.
- **Adenomatous polyp syndromes**:
    - Added expansive criteria to include individuals with multifocal or bilateral congenital hypertrophy of retinal pigment epithelium (CHRPE).
    - Added expansive criteria to include first-, second-, or third-degree relatives with known pathogenic variant or clinical findings suggestive of an inherited polyposis syndrome.
- **Juvenile polyposis syndrome**: Increased testing requirement for number of juvenile polyps in the colon from three to five (restrictive).
- **Cowden syndrome**: Expanded minor criteria to include colorectal cancer and lipomas to the list of conditions that may be present.
- **Lynch syndrome**: Personal history criteria expanded to include any Lynch syndrome related cancer: colorectal, endometrial, gastric, ovarian, pancreatic, urothelial, CNS glioma, biliary tract, small intestine, sebaceous adenomas or carcinomas, keratoacanthomas, or breast carcinomas with medullary features.
- **Li-Fraumeni syndrome**:
    - Expanded the personal history criteria to include pediatric hypodiploid acute lymphoblastic leukemia.
    - Restricted germline testing criteria for testing as follow-up to TP53 positive somatic tumor test results as per ASCO guideline.
    - Restricted germline testing criteria for testing of unaffected first-, second-, or third-degree relatives to individuals whose affected relative meets LFS personal history criteria.
- **Hereditary Breast Cancer**:
    - Expanded BRCA1/2 testing criteria to include all women <65 with personal history of breast cancer.
    - All individuals who are candidates for PARP inhibitor therapy are included in scope for testing.
    - Clarified the statement about BRCA risk models, eliminating reference to tools that are not examples of validated risk models.

    - Family history criteria for testing related to having a relative with multiple primary breast cancers expanded to first- or second-degree relative.
    - Family history criteria for testing related to having a relative with epithelial ovarian, fallopian tube, or primary peritoneal cancer expanded to include first-, second-, or third-degree relatives.
    - Family history criteria for testing related to having a relative with breast cancer who is also an individual assigned male sex at birth expanded to include first-, second-, or third-degree relatives.
    - Family history criteria for testing related to having a relative age <50 with breast cancer expanded to be at least one relative who is a first-, second-, or third-degree blood relative.
- **Hereditary epithelial ovarian cancer**: Clarified the statement about BRCA risk models, eliminating reference to tools that are not examples of validated risk models.
- **Hereditary pancreatic ductal adenocarcinoma**: Clarified the statement about BRCA risk models, eliminating reference to tools that are not examples of validated risk models.
- **Multi-gene panel testing for HBOP**:
    - For pancreatic carcinoma, expanded the multi-gene panel list to include CDK4.
    - For breast cancer, removed the following genes from the multi-gene panel list: ATM, BARD1, CHEK2, RAD51C, and RAD51D.
- **Melanoma**: Gene list expanded to 20 genes and can include CDK4 pathogenic variants.
- **Nevoid basal cell carcinoma syndrome**:
    - Expanded threshold for number of basal cell carcinomas from 5 in a lifetime to as low as two (multiple) if this is considered out of proportion to prior skin exposure or skin type.
    - Removed age restriction for Lamellar calcification of the falx cerebri (major criterion).
- **Endocrine neoplasms**: Expanded criteria to include early onset GI stromal tumors to account for evaluation for SDHB gene-deficient GIST.
- **Kidney cancer**:
    - Expanded criteria to include individuals with a personal history of various rare kidney tumors (Birt-Hogge-Dubé syndrome, HLRCC associated renal cell carcinoma, etc.).
    - Expanded criteria to include unaffected individuals with two or more first- or second-degree relatives with renal cell carcinoma.

- **Prostate Cancer**:
    - For individuals with low-risk prostate cancer, criteria expanded to include family history of breast cancer in relatives assigned female at birth and age ≤50; family history of pancreatic, gastric, brain, melanoma, intestinal (colorectal or small bowel), or endometrial cancer diagnosed at age ≤50; family history of upper tract urothelial cancer(s) in first- or second-degree relatives; Ashkenazi Jewish ancestry; intraductal or cribriform histology.
    - For individuals with intermediate risk prostate cancer, criteria expanded to include family history of breast cancer in relatives assigned female at birth and age ≤50; family history of pancreatic, gastric, brain, melanoma, intestinal (colorectal or small bowel), or endometrial cancer diagnosed at age ≤50; family history of upper tract urothelial cancer(s) in first- or second-degree relatives.
    - Removed CHEK2 or PALB2 from the multi-panel gene list for prostate cancer.
    - Expanded family history criteria to first-, second-, or third-degree relatives with multiple primary breast cancers.
    - Expanded family history criteria of prostate cancer diagnosed before age 60 to include at least one first- or second-degree relative.
    - For individuals unaffected by prostate cancer, criteria are expanded to include 11 additional family history indicators for risk of BRCA1 or BRCA2 pathogenic variants that match the hereditary breast cancer family history criteria.
    - Clarified the statement about BRCA risk models, eliminating reference to tools that are not examples of validated risk models.

For questions related to guidelines, contact Carelon via email at MedicalBenefitsManagement.guidelines@Carelon.com, or download a copy of the current and upcoming guidelines.