Sentara Health Plans

Commercial

Genetic Testing-Cancer Prevention, Diagnosis and Treatment, Medical 34A

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Coverage Policy	Medical 34A
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Member-specific benefits take precedence over medical policy and benefits may vary across plans. Refer to the individual's benefit plan for details *.

Purpose:

This policy addresses various single and panel genetic testing for cancer prevention, diagnosis and treatment.

Description & Definitions:

Hereditary cancer is a cancer that has developed as a result of a gene mutation passed down from a parent to a child. Inheriting a gene mutation does not necessarily mean that person will develop cancer, but increases their risk.
Research and studies have found that certain gene mutations increase the chances of a person to develop certain kinds of cancers, depending on family history, or to respond to certain therapies for cancer, based on the genetic components of the tumor.

Autosomal recessive: A genetic condition that appears only in individuals who have received two copies of an autosomal gene, one copy from each parent. The gene is on an autosome, a non-sex chromosome. The parents are carriers who have only one copy of the gene and do not exhibit the trait because the gene is recessive to its normal counterpart gene.

X-linked recessive inheritance - hereditary pattern in which a recessive gene on the X chromosome results in the manifestation of characteristics in male offspring and a carrier state in female offspring.

A **first-degree** relative is defined as a relative which includes the individual's parents, full siblings, or children

A **second-degree** relative is defined as a blood relative which includes the individual's grandparents, grandchildren, aunts, uncles, nephews, nieces or half-siblings

A **third-degree** relative is defined as a blood relative which includes the individual's first-cousins, great-grandparents or great grandchildren

Criteria:

Genetic Testing is considered medically necessary for the prevention, diagnosis and treatment of cancer of patients who meet **ALL** the following:

- There is an approved mutation specific treatment available

- There is sufficient Published Scientific Evidence or 3rd party Consensus in the Medical Community that the results of the specific genetic Testing directs clinical management and improves clinical outcomes;
- After completion of a thorough history, physical examination, pedigree analysis, genetic counseling, relevant diagnostic and biochemical tests (if any), the patient meets criteria for **1 or more** of the following approved tests:
    - **BRCA1 and BRCA 2 and BRCA Analysis Rearrangement Testing (BART)** is medically necessary for **1 or more** of the following:
        - BRCA testing is covered without preauthorization
        - BRCA Analysis Rearrangement Testing (BART) is covered without preauthorization.
        - Additional Genes ATM, CDH1, CHEK2, PALB2, PTEN, STK11, and/or TP53 may be testing in individuals over the age of 18 who meet **1 or more** of the following clinical indications when the test results are used to make clinical management decisions:
            - Biologically-related individual from a family with a known BRCA1, BRCA2, ATM, CDH1, CHEK2, PALB2, PTEN, STK11, and/or TP53 mutation
            - Individual personal history of breast cancer and **1 or more** of the following:
                - Diagnosed at age 45 or younger
                - Diagnosed at age 50 or younger with **1 or more** of the following:
                    - An additional breast cancer primary
                    - At least one close blood relative with breast cancer at any age
                    - At least one close blood relative with epithelial ovarian, fallopian tube, or primary peritoneal cancer
                    - At least one close blood relative with pancreatic cancer
                    - At least one close blood relative with prostate cancer (Gleason score greater than or equal to 7)
                    - An unknown or limited family history (e.g. fewer than two first- or second-degree female relatives or female relatives surviving beyond 45 years in the relevant maternal and/or paternal lineage
                - Diagnosed at age 60 or younger with a triple negative breast cancer (ER, PR and HER)
                - Diagnosed at any age with **1 or more** of the following:
                    - At least one close blood relative with breast cancer diagnosed at age 50 or younger
                    - At least two close blood relatives with breast cancer at any age
                    - At least one close blood relative with epithelial ovarian, fallopian tube, or primary peritoneal cancer
                    - At least two close blood relatives with pancreatic cancer and/or prostate cancer (Gleason score greater than or equal to 7) at any age
                    - At least one close male blood relative with breast cancer
                    - Individual of Ashkenazi Jewish descent, no additional family history required
            - Individual personal history of epithelial ovarian, fallopian tube, or primary peritoneal cancer at any age
            - Individual personal history of male breast cancer at any age
            - Individual with a personal history of pancreatic cancer at any age, who have at least one close blood relative on the same side of the family with **1 or more** of the following:
                - Breast cancer at age 50 or younger
                - Ovarian cancer at any age
                - Pancreatic cancer at any age
            - Individual of Ashkenazi Jewish descent, no additional family history required;
            - Individual with a personal history of prostate cancer (Gleason score greater than or equal to 7) at any age with at least one close blood relative with **1 or more** of the following:
                - Breast cancer at age 50 or younger
                - Ovarian cancer at any age
                - Pancreatic cancer at any age
                - Prostate cancer (Gleason score greater than or equal to 7) at any age

- No personal history of breast or ovarian cancer and a family history of first- or second-degree blood relative meeting **any of the above criteria**;
- No personal history of breast or ovarian cancer and a family history of a third-degree blood relative with breast and/or epithelial ovarian/fallopian tube/primary peritoneal cancer with two or more close blood relatives with breast and/or ovarian cancer (with at least one close blood relative with breast cancer prior to age 50).
- Individuals with a combination of breast cancer with **1 or more** of the following:
    - Thyroid cancer
    - Sarcoma
    - Adrenocortical Cancer
    - Endometrial cancer
    - Pancreatic cancer
    - Brain tumors
    - Gastric cancer
    - Leukemia
    - Lymphoma

- **Familial Adenomatous Polyposis (FAP) or attenuated familial adenomatous polyposis (AFAP)** is medically necessary **1 or more** of the following:
    - To confirm the diagnosis of FAP in an affected patient
    - To provide presymptomatic testing for at -risk relatives (first- or second- or third degree relative) of an affected patient
    - To confirm the diagnosis of FAP in those with 10 or more adenomas
    - To provide presymptomatic testing for at -risk relatives (first- or second- or third degree relative) of an affected patient
- **Colaris, COLARIS AP and/or MUTYH, APC, MLH1, MSH2, MSH6, PMS2, EPCAM, MYH** gene testing (1, 2 or 3) must meet **1 or more** of the following criteria:
    - Individual should meet **ALL** of the following criteria based on Amsterdam criteria combined I and II (based on family history)
        - At least three relatives with CRC or with an HNPCC-associated cancer (colorectal cancer, endometrial cancer, ovarian cancer, cancer of the stomach, small bowel, pancreas, ureter or renal pelvis, biliary tract, brain/CNS, sebaceous gland adenomas or keratocanthomas as seen in Muir-Torre syndrome);
        - One member should be a first degree relative of the other two
        - At least two successive generations should be affected;
        - At least one member should be diagnosed with Colorectal Cancer or a cancer associated with Lynch syndrome (colorectal cancer, endometrial cancer, ovarian cancer, cancer of the stomach, small bowel, pancreas, ureter or renal pelvis, biliary tract, brain/CNS, sebaceous gland adenomas or keratocanthomas as seen in Muir-Torre syndrome); before age 50
    - Member should meet **1 or more** of the following criteria based on revised **Bethesda guidelines** (based on **personal history)**
        - Colorectal cancer diagnosed in an individual younger than 50 years;
        - Presence of synchronous or metachronous, colorectal or other Lynch-Syndrome related tumor (colorectal cancer, endometrial cancer, ovarian cancer, cancer of the stomach, small bowel, pancreas, ureter or renal pelvis, biliary tract, brain/CNS, sebaceous gland adenomas or keratocanthomas as seen in Muir-Torre syndrome); regardless of age
        - Colorectal cancer with MSI-high (MSI-H) pathologic –associated features diagnosed in an individual younger than 60 years (i.e, presence of tumor infiltrating lymphocytes, Crohn's like lymphocytic reaction, mucinous/signet -ring differentiation, or medullary growth pattern);
        - Colorectal cancer or Lynch syndrome-associated tumor (colorectal cancer, endometrial cancer, ovarian cancer, cancer of the stomach, small bowel, pancreas, ureter or renal pelvis, biliary tract, brain/CNS, sebaceous gland adenomas or keratocanthomas as seen in Muir-Torre syndrome); diagnosed in a member AND in at least one first degree relative younger than 50 years;
        - Colorectal cancer or Lynch syndrome-associated tumor (colorectal cancer, endometrial cancer, ovarian cancer, cancer of the stomach, small bowel, pancreas, ureter or renal pelvis, biliary tract, brain/CNS, sebaceous gland adenomas or

keratocanthomas as seen in Muir-Torre syndrome); diagnosed in a member AND in at least two first or second degree relatives at any age
- For a member from a family with known high risk syndrome associated with colorectal cancer, with or without known mutation,
- Member with a desmoid tumor

- Lynch syndrome testing in patients with at least a 5% risk to carry a mutation using **1 or more** of the following Lynch Syndrome Risk Assessment models:
  - PREMM 1,2,6: http://premm.dfci.harvard.edu/
  - MMR Predict: https://webapps.igc.ed.ac.uk/world/research/hnpccpredict/
  - MMRPro – submit clinical information

- **KRAS and NRAS Testing** is medically necessary for **1 or more** of the following:
  - If currently being considered for treatment with Erbitux® (cetuximab) or Vectibix™ (panitumumab) for colorectal cancer
  - Before beginning Erbitux or Vectibix treatment, either as single medicines or in combination with chemotherapy
  - When first diagnosed with advanced colon or rectal cancer and are planning a treatment strategy
  - Individual with metastatic colorectal Cancer (CRC) needing tumor tissue genotyping for RAS mutations both KRAS and NRAS.
- **Multiple Endocrine Neoplasia Type 1(MEN1) or RET gene** testing is medically necessary for **1 or more** of the following:
  - Clinical suspicion or family history of multiple endocrine neoplasia syndrome, as indicated by **1 or more** of the following
    - Patient with 2 or more endocrine tumors
    - Patient with family history of 2 or more endocrine tumors
    - Patient with "red flag" tumor, as indicated by **1 or more** of the following:
      - Medullary carcinoma of thyroid
      - Pheochromocytoma
      - Parathyroid carcinoma;
      - Paraganglioma
    - MEN1 testing in patient with **1 or more** of the following:
      - Appropriate primary hyperparathyroidism feature, as indicated by **1 or more** of the following
        - Multiglandular hyperparathyroidism;
        - Onset of primary hyperparathyroidism at age 30 years or younger
        - Relative with primary hyperparathyroidism
      - Gastrinoma
      - Multifocal pancreatic endocrine tumors
      - Relative of patient with known MEN1 mutation
- **Medullary Thyroid Cancer and Multiple Endocrine Neoplasia Type 2 (MEN2), RET** testing is medically necessary for **1 or more** of the following:
  - Among members of families with defined RET gene mutations
  - Among members of families known to be affected by inherited medullary thyroid cancer but not previously evaluated for RET mutation
  - In members with sporadic medullary thyroid cancer.
- **Molecular and/or gene expression classifiers for molecular markers for the evaluation of thyroid nodules** for **1 or more** of the following:
  - Thyroid Cancer Mutation Panel (BRAF, RAS, RET/PTC, PAX8/PPAR) when the result of fine needle aspiration sampling of the thyroid nodule is indeterminate
  - Afirma test is considered medically necessary unless there is evidence of the lesion being clearly benign or malignant
  - ThyroSeq Panel is medically necessary for **1 or more** of the following:
    - This test is considered medically necessary when there is a follicular or Hürthle cell neoplasm
    - Atypia of undetermined significance or follicular lesion of undetermined significance
- **Oncotype DX for Breast Cancer - Reverse transcriptase polymerase chain reaction assay for breast cancer gene expression (Oncotype DX)** is indicated when **ALL** of the following are present:

- Axillary node biopsy is negative for tumor or Tumor is pN0 (node negative) or pN1mi with axillary lymph node micrometastasis less than or equal to 2mm; or with 1-3 positive Axillary Lymph Nodes (ALN) (e.g., Oncotype DX for ductal carcinoma in situ without DCIS recurrence score);
- Newly diagnosed invasive ductal or invasive lobular carcinoma of breast, stage I or II
- The outcome of testing will guide decision making regarding adjuvant chemotherapy;
- Patient is female
- Primary tumor is estrogen receptor-positive
- Primary tumor is HER-2 receptor-negative.

- **TP53 gene testing** for individuals with 1 or more of the following:
  - Individual with a suspected or known clinical diagnosis of Li-Fraumeni syndrome (LFS)
  - Li-Fraumeni-Like syndrome, or a known family history of a P53 mutation
  - Individual whose medical and/or family history is consistent with **1 or more** of the following:
    - A relative with a known deleterious TP53 gene mutation
    - A diagnosis of classic Li-Fraumeni syndrome, defined by **ALL** of the following:
      - Diagnosis of sarcoma before the age of 45 years
      - A parent, child, or full sibling diagnosed with cancer before the age of 45 years;
      - An additional first- or second-degree relative in the same lineage with cancer diagnosed before age 45 years, or a sarcoma at any age;
    - A diagnosis of Li-Fraumeni-Like syndrome defined by **ALL** of the following:
      - Diagnosis of a childhood tumor or sarcoma, brain tumor, or adrenocortical carcinoma diagnosed before age 45 years;
      - A first- or second-degree relative with typical Li-Fraumeni syndrome tumor* at any age;
      - Another first- or second-degree relative with cancer diagnosed before age 60 years;
    - A diagnosis of breast cancer before age 35 years with a negative BRCA1/2 test especially if there is a family history of sarcoma, brain tumor or adrenocortical carcinoma.
  - For individual with multiple primary tumors, 2 of which are sarcoma, brain or breast cancer and/or adrenocortical cancer before age 36
  - Individual with adrenocortical cancer and choroid plexus ca at any age
- **PTEN Gene testing** should meet criteria for either Operational Diagnosis in member or Operational diagnosis for family where one individual is diagnostic for Cowden Syndrome as evidence by **1 or more** of the following (See below criteria for **Pathognomic Criteria, Major Criteria** and **Minor Criteria** definitions[#]):
  - Operational Diagnosis in individual as evidence by **1 or more** of the following:
    - Mucocutaneous lesions alone with **1 or more** of the following:
      - There are 6 or more facial papules, of which 3 or more must be trichilemmoma;
      - Cutaneous facial papules and oral mucosal papillomatosis
      - Oral mucosal papillomatosis and acral keratoses
      - Palmoplantar keratoses, 6 or more
    - Two or more major criteria but one must include macrocephaly or Lhermitte-Duclos disease (LDD)
    - 1 major and 3 minor criteria
    - 4 minor criteria
  - Operational diagnosis in a family where one person is diagnostic for Cowden syndrome as evidence by **1 or more** of the following:
    - Any pathognomonic criterion
    - Any one major criterion with or without minor criteria
    - Two minor criteria
    - History of Bannayan-Riley-Ruvalcaba syndrome
- **MYH-associated polyposis (MAP)** is appropriate when **1 or more** of the following criteria is met:
  - Members with greater than 10 adenomatous colonic polyps; or greater than 15 cumulative adenomas in 10 years and have either
    - Who have a recessive inheritance (family history positive only for siblings)
    - Who have undergone testing for adenomatous polyposis coli (APC) with negative results

        - The asymptomatic siblings of individuals with known MYH-associated polyposis (MAP) and/or Colon Cancer.
    - **BCR-ABL mutation analysis** is medically necessary for **1 or more** of the following:
        - BCR-ABL and T315-I mutation analysis is covered for the diagnosis and management of members with Philadelphia chromosome positive (Ph+) Chronic Myelogenous Leukemia (CML), or acute lymphoblastic leukemia (ALL)
        - As part of the workup for myelodysplastic syndrome (MDS) myeloproliferative neoplasm (MPN) that includes persistent leukocytosis, thrombocytosis, or cytopenias
        - BCR-ABL mutation other than T315-I for patients considered for treatment with dasatinib (Sprycel®) or nilotinib (Tasigna)
    - **Pathfinder TG** is medically necessary for **1 or more** of the following:
        - To be used adjunctively in cases in which a definitive pathologic diagnosis cannot be rendered on a tissue or cytology specimen, either due to inadequate specimen or equivocal histologic or cytologic findings
    - **Genetic testing for susceptibility to malignant diseases** not listed above is covered when **ALL** of the following criteria are met:
        - The genetic disorder is associated with a potentially significant cancer or has a lethal natural history;
        - The risk of the type of cancer from the genetic disorder cannot be identified through biochemical or other testing
        - Specific mutation(s) have been established in the scientific literature to be reliably associated with the disease;
        - The results of the genetic test may impact the medical management of the individual;
        - Testing is accompanied by genetic counseling
    - **Von Hippel-Lindau syndrome (VHL) gene** testing when **ALL** of the Following:
        - The member displays clinical features, or is at direct risk of inheriting the mutation in question (pre-symptomatic)
        - The result of the test will directly impact the treatment being delivered to the member;
        - After history, physical examination, pedigree analysis, genetic counseling, and completion of conventional diagnostic studies, a definitive diagnosis remains uncertain
    - **CBFB/MHY 11(acute myeloid leukemia)** to diagnose acute myelomonocytic leukemia (AML) with abnormal eosinophils covered without criteria.
    - **KIT Test (9C Kit/V Kit Hardy Zuckerman Oncogene)** for Gastrointestinal Stromal Tumor (GIST) is covered without criteria.
    - **BRAF gene** is covered without criteria.
    - **FLT3 (fms-related tyrosine kinase 3)/ CEBPA/ NPM1** (This test may also be ordered as a soft FLDV) is medically necessary for any individual diagnosed with acute myeloid leukemia.
    - **STK11** is medically necessary for **All** of the following:
        - Individual with harmatomatous polyps
        - breast cancer with hyperpigmented macules of the lip and oral mucosa
    - **CDH1** gene testing is medically necessary for **1 or more** of the following:
        - ≥2 cases of diffuse gastric cancer in first degree relatives, with at least one diagnosed at <50 years
        - ≥3 cases of documented diffuse cancer in first or second degree relatives independent of age of onset
        - Personal history of diffuse gastric cancer diagnosed at <40 years regardless of family history;
        - A personal or family history of diffuse gastric cancer **AND** lobular breast cancer with one diagnosed at <50 years
    - **JAK2 (including exons 12 and 13 or JAK2V617F)**, **Myeloproliferative Leukemia gene (MPL)**, and **Calrecticulin Mutation Analysis (CALR)** gene testing is medically necessary for **1 or more** of the following:
        - $JAK2^{V617F}$, MPL, and/or CALR for initial testing of clinical and laboratory features suggestive of polycythemia vera
        - Clinical, laboratory, and/or bone marrow features suggestive of essential thrombocytosis
        - Clinical, laboratory, and/or bone marrow features suggestive of primary myelofibrosis (chronic leukemia) or leukocytosis.
        - JAK2 tyrosine kinase mutation (e.g., in exon 12) testing when $JAK2^{V617F}$ testing is negative
    - **Immuno Globulin Heavy Chain (IGH)** is medically necessary for the diagnosis and management of patients with 1 or more of the following:
        - Multiple Myeloma

        - Status post Bone Marrow /Stem Cell Transplantation
        - Acute myeloid leukemia (AML), also known as acute myelogenous leukemia or acute nonlymphocytic leukemia (AML or ANLL)
    - **PML/RAR Alpha (Promyelocytic Leukemia - PML-RAR alpha PCR)** testing for **1 or more** of the following**:**
        - at the end of consolidation treatment
        - Relapse monitoring – (e.g. every 3 months for 2 years or every 3-6mo for the next 3 years)
        - if a positive test result is obtained, repeat testing from bone marrow in 2-4wks
        - high risk members >60y/o or who had interruptions during consolidation or not able to tolerate maintenance
    - **Hereditary retinoblastoma, RB1 Testing** for diagnosis or screening for hereditary retinoblastoma, as indicated by **1 or more** of the following
        - First-degree relative of patient with known RB1 mutation
        - Patient with retinoblastoma, with or without family history of retinoblastoma
    - **Calreticulin Exon 9 (CALR) testing** is covered **without** criteria or preauthorization.
    - **Epidermal growth factor receptor (EGFR)** [for example, Therascreen] is considered medically necessary as a technique to predict treatment response for individuals with non-small cell, non-squamous cell lung cancer undergoing treatment with EGFR tyrosine kinase inhibitor therapy (for example, erlotinib [Tarceva], gefitinib [Iressa], or afatinib [Gilotrif]).
    - **ALK gene** is approved for members with lung cancer or for consideration of treatment of **any** drug which requires ALK gene testing as part of FDA indication.
    - **Juvenile polyposis syndrome (JPS SMAD4 and BMPR1A)** is covered for individuals with 1 or more of the following:
        - Have five or more juvenile polyps in the colorectum
        - any juvenile polyps in other parts of the gastrointestinal tract
    - **Bladder Tumor Marker Testing (e.g. UroVysion, bladder tumor antigen test, nuclear matrix protein 22 testing (NMP-22)**, or fibrin/fibrinogen degradation products test) is considered medically necessary for **1 or more** of the following:
        - Follow-up of treatment for bladder cancer
        - Monitoring for eradication of bladder cancer
        - Recurrences after eradication
    - **Bone marrow testing for MYD88 gene mutation** is covered for individuals being evaluated for Waldenström Macroglobulinemia or Lymphoplasmacytic Lymphoma.
    - **Hereditary Paraganglioma-Pheochromocytoma (PGL/PCC) Syndrome** testing is medically necessary for **1 or more** of the following:
        - Individual has a first-degree relative with a known SDHB, SDHC, SDHD, or TMEM127 mutation
        - Individual with paraganglioma or pheochromocytoma characterized by **1 or more** of the following:
            - Malignant tumor
            - Previous head and neck paraganglioma (e.g., carotid body tumor)
            - Recurrent tumor
            - Tumor diagnosed before age 45 years
            - Two or more metachronus (diagnosed at different times) tumors
        - Individual with pheochromocytoma without clinical findings suggestive of neurofibromatosis type 1, von Hippel-Lindau syndrome, or multiple endocrine neoplasia type 2.
    - **Endopredict Panel Testing** is medically necessary for anyone who has already had the oncotype Dx and is considering additional chemo and/or hormonal therapy where the results would help informed treatment.
    - **Mammaprint** is medically necessary for **All** of the following:
        - Breast tumor is anatomic stage 1 or stage 2
        - Histologic type is ductal, lobular, mixed (ductal/lobular), or metaplastic
        - Node negative OR 1-3 positive node breast cancer
        - Breast tumor is estrogen receptor positive and/or progesterone receptor positive
        - Breast tumor is HER2-negative
        - Patient is a candidate for chemotherapy (i.e., chemotherapy not precluded due to other factors)

        - Adjuvant chemotherapy is being considered and this testing is being ordered to assess recurrence risk to guide decision making as to whether or not adjuvant chemotherapy will be utilized
    - **Decipher®** may be covered for **All** of the following:
        - Individual has not had previous tumor-based assay (Prolaris®, Oncotype DX®, Promark®, OR Decipher®) to guide management of prostate cancer in individual's lifetime
        - Individual is a candidate for definitive therapy or active surveillance
        - life expectancy greater than 10 years
        - PSA persistence after radical prostatectomy
        - PSA recurrence after radical prostatectomy
        - Individual must fall into **1** of the following stages:
            - Low Risk
            - Favorable Intermediate Risk
            - Unfavorable intermediate
            - High-risk
    - **OncotypDX for Prostate** may be covered by All of the following:
        - Individual has not had previous tumor-based assay (Prolaris®, Oncotype DX®, Promark®, OR Decipher®) to guide management of prostate cancer in individual's lifetime
        - Individual is a candidate for definitive therapy or active surveillance
        - life expectancy of greater than 10 years
        - Individual must fall into **1** of the following stages:
            - Very Low Risk
            - Low Risk
            - Favorable Intermediate Risk
    - **Prolaris®** may be covered for **ALL or more of the** following:
        - Individual has not had previous tumor-based assay (Prolaris®, Oncotype DX®, Promark®, OR Decipher®) to guide management of prostate cancer in individual's lifetime
        - Individual is a candidate for definitive therapy or active surveillance
        - life expectancy of greater than 10 years
        - Individual must fall into **1** of the following stages:
            - Low Risk
            - Favorable Intermediate Risk
            - Unfavorable intermediate
            - High-risk
    - **ProMark® Risk Score** may be covered for **All** of the following:
        - Individual has not had previous tumor-based assay (Prolaris®, Oncotype DX®, Promark®, OR Decipher®) to guide management of prostate cancer in individual's lifetime
        - Individual is a candidate for definitive therapy or active surveillance
        - life expectancy of greater than 10 years
        - Individual must fall into **1** of the following stages:
            - Low Risk
            - Favorable Intermediate Risk
    - **ExoDX Prostate (EPI, ExosomeDx Prostate, IntelliScore)** is considered medically necessary once in an individual's lifetime with **1 or more** of the following criteria:
        - Individual with PSA >3.0 ng/mL with or without previous benign prostate biopsy
        - Individual with Digital rectal exam suspicious for cancer
    - **Signatera (liquid biopsy minimal residual disease)** testing is considered medically necessary for **1 or more** of the following:
        - Individual previously diagnosed with Colorectal cancer
    - **CSF3R gene** is covered for individual with **1 or more** of the following:
        - Asymptomatic Individuals with persistent, moderately elevated neutrophil counts
        - History of Severe congenital neutropenia (SCN)
        - Molecular testing of peripheral blood to detect chromosomal abnormality for diagnosis of **1 or more** of the following:
            - Atypical chronic myeloid leukemia (aCML)
            - Acute MYELOID leukemia (AML)

- Chronic neutrophilic leukemia (CNL)
- Myelodysplastic Syndromes as evidence by **1 or more** of the following:
  - MDS
  - myelodysplasia
  - pre-leukemia
  - refractory anemia

▪ Evidence needed for the use for Ruxolitinib

- **ClonoSEQ** testing is considered medically necessary for individuals with **1 or more** of the following:
  - acute lymphocytic leukemia (ALL)
  - multiple myeloma (MM)
  - chronic lymphoblastic leukemia (CLL)
  - B-Cell Lymphoma
- **Breast Cancer Index (BCI)** testing is considered medically necessary to assess the risk for recurrence in an individual when **All** of the following criteria are met:
  - Individual has undergone surgery and/or full pathological staging prior to testing
  - There is no evidence of distant metastatic breast cancer
  - Breast cancer is nonmetastatic (node negative) or with 1-3 involved ipsilateral axillary lymph nodes
  - Breast tumor is estrogen receptor and/or progesterone receptor positive
  - Breast tumor is HER2 receptor negative
  - Postmenopausal or 50 years of age
  - Patient is a candidate for chemotherapy or endocrine therapy
  - Adjuvant chemotherapy is being considered and this testing is being ordered to assess recurrence risk to guide decision making as to whether or not adjuvant chemotherapy will be utilized
  - No more than one predictive Gene Expression Test for the same breast tumor has been performed
- **Guardant360® CDx** comprehensive Liquid Biopsy is medically necessary with **All** of the following:
  - Solid tumor or hematologic tumor type with **1 or more** of the following:
    - Tissue block if available
    - Liquid biopsy if tissue not possible
    - Repeat testing on a new tissue or liquid biopsy for progressive or relapse disease.
- **Tumor testing or liquid biopsy** (IE: FoundationOne CDx, FoundationOne Liquid CDx, Guardant, Caris, Tempus by Foundation Medicine, Myriad: Precise Tumor) testing may be indicated when **1 or more** of the following are present:
  - For tissue-based testing with **ALL** of the following:
    - For Patient diagnosed with solid tumor malignancy (eg, breast, cervical, colorectal, non-small cell, pancreatic, prostate, sarcoma, thyroid)
    - Systemic targeted therapy being considered (eg, crizotinib, erlotinib, olaparib, pembrolizumab, vemurafenib), and FDA-approved prescribing drug label requires use of biomarker from this assay to effectively use the therapy in specific cancer or tumor type
  - For when tissue-based testing is infeasible(i.e., quantity not sufficient for tissue-based test or invasive biopsy is medically contraindicated) with **ALL** of the following:
    - An individual being considered for ICI targeted therapy, liquid biopsy based TMB and/or MSI testing for the solid tumors
    - Systemic targeted therapy being considered (eg, crizotinib, erlotinib, olaparib, pembrolizumab, vemurafenib), and FDA-approved prescribing drug label requires use of biomarker from this assay to effectively use the therapy in specific cancer or tumor type
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Pathognomic Criteria, Major Criteria and Minor Criteria definitions

Pathognomonic criteria:

- Mucocutaneous lesions:
  - Trichilemmomas, facial
  - Acral keratoses
  - Papillomatous lesions

    - Mucosal lesions
- Adult Lhermitte-Duclos disease (LDD)(cerebellar tumors)

Major criteria:

- Breast carcinoma
- Follicular thyroid cancer
- Macrocephaly (eg, 97th percentile) (megalocephaly)
- Endometrial cancer

Minor criteria:

- Other thyroid lesions (eg, goiter, adenomas)
- Mental retardation (ie, IQ 75)
- GI hamartomas
- Fibrocystic disease of the breast
- Lipomas
- Fibromas
- GU tumors (especially renal cell carcinoma), GU structural manifestations
- Uterine fibroids or malformation
- Colon cancer,
- Esophageal glycogenic acanthosis,
- Papillary or follicular variant of papillary thyroid cancer,
- Testicular lipomatosis,
- Vascular anomalies (including multiple intracranial developmental venous anomalies).

Effective 2/28/2023, genetic panels of not more than 75 genes are approved for cancer management and treatment. Please disregard any exceptions below that contradict this.

The following genetic panels are considered **not medically necessary** for any use other than those indicated in clinical criteria, to include but not limited to:

- 4K score
- Ambry's PCDNext panel
- Amsterdam
- Archer DX FusionPlex Kits for blood cancer assays, oncology Research Panel, Thyroid Panel, Solid Tumor Panel, ALK, RET, ROS1 Panel, Sarcoma Panel, NTRK Panel, FGFR Panel, and My Fusion Plex kit
- bioTheranostics Cancer Type ID
- BluePrint™ (also referred to as "80-gene profile")
- Bone Marrow Failure Syndrome
- Bone Marrow Targeted Genomic Sequencing by Trusight for Acute Myeloid Leukemia
- Breast Cancer Gene Expression Ratio (Theros H/I)
- BreastNext panel,
- BreastOncPX™
- BreastPRS
- Brevagen
- CancerNext Genetic Testing
- Chemo FX Assay test - Precision Therapeutics
- Chromosome 3 Gene Test for myeloid disorders
- Circulating microRNAs (e.g., miR-1, miR-16, miR-26a, miR-27a, and miR-29a, miR-133a, and miR-199a-5p; not an all-inclusive list)
    - Oncology (thyroid), microRNA profiling by RT-PCR of 10 microRNA sequences, utilizing fine needle aspirate, algorithm reported as a positive or negative result for moderate to high risk of malignancy
    - Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score
    - MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
    - MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
    - MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
    - PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA

sequence analysis (List separately in addition to code for primary procedure)
    - Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)
- ColoSeq
- Colonext
- ColonSentry
- ConfirmMDx
- CxBladder
- DecisionDx: all Decision DX tests including Cutaneous Melanoma, Esophageal Cancer, Mesothelioma, and Glioblastoma Multiforme
- DetermaRX
- DermTech Pigmented Lesion Assay (PLA)
- Digene HPV test
- Duke University Colon Hotspot NGS panel
- Exome Sequence Analysis
- Foundation One® Heme lab test
- GeneDX OncoGene Dx panel
- Genome Sequence Analysis
- Genomic grade index,
- Immunoscore Colon test
- Insight® DX Breast Cancer Profile
- Know error system (Forensic testing)
- LungLB®
- MammaTyper®
- Mammostrat
- Mammostrat
- Melaris test
- Microculture Kinetic (MiCK) Apoptosis Assays (e.g., Correct Chemo assay)
- MyPRS test
- myPath
- myRisk
- NexCourse® Breast IHC4
- NPI+ and Randox Breast Cancer Array
- NuvoSelect™ eRx 200-Gene Assay
- Oncomap™ ExTra
- Oncotype DX Breast Cancer Assay with DCIS recurrence score
- Oncotype DX for Colon Cancer
- Oncotype DX for lobular carcinoma in situ (LCIS)
- OnDose
- OvaNext Next Generation Sequencing Panel
- PancraGen panel
- Pathwork Tissue of Origin test or the Pathwork Tissue of Origin test kit
- Percepta Bronchial Genomic Classifier
- Pervenio Lung RS panel
- PGDx
- PreOvar test
- Prosigna Breast Panel
- Rotterdam
- SelectMDx
- SYMPHONY™ Genomic Breast Cancer Profile
- Target Now
- TargetPrint®
- The 41-gene signature assay.
- The 76-gene "Rotterdam signature" assay
- TheraGuide 5-FU
- TheraPrint ™
- THEROS Breast Cancer Index
- VeriStrat
- VistaSeq panel
- Whole Exome Sequencing (WES);
- Whole Genome Sequencing

The following genes are considered **not medically necessary** for any use other than those indicated in clinical criteria, to include but not limited to:

- ATK1
- AXIN2
- BAG1
- BARD1
- BIRC4
- BDX-XL2
- BRIP1
- CEACAM6
- CDC6
- CDK2AP1
- CDK4
- CDKN2A
- CSF1R
- CTNNA1
- CTNNB1
- DDR2
- ELANE(ELA2 test),
- ERBB2
- ERBB3
- ERBB4
- ESD
- FBXW7
- FGFR1
- FGFR2
- FGFR3
- FH (fumarate hydratase)
- FUT3
- GALNT12
- GNAQ
- GNAS
- GREM1
- Home genetic testing
- HRAS
- IDH1/2 Gene
- IGK (Immunoglobulin Kappa Light Chain Locus)
- IL11
- KDR
- KIR TYPING (killer immunoglobulin like receptor)
- LCK
- MAP2K1
- MET amplifications (e.g., cMET)
- MITF (microphthalmia-associated transcription factor)

- MRE11
- MRE11A
- MYCN gene
- MyPath Melanoma
- NBN
- NOTCH1
- PAM50
- PDGFR
- PIK3CA
- POLD1
- POLE
- PRKAR1A
- PCA3 Gene
- UpM3
- PTCH1
- RAD50
- RAD51C
- RAD51D
- Repeat/Duplicative genetic testing
- RND3
- ROS1 gene mutations
- RPS20
- SEPT9
- SH3BGR
- TCD
- TERT
- TPB
- TRB@/TRG@
- WNT3A
- XRCC2
- YAP

Coding:

Medically necessary with criteria:

Coding	Description
81162	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (ie, detection of large gene rearrangements)
81163	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81164	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81165	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81166	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full duplication/deletion analysis (ie, detection of large gene rearrangements)
81170	ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase) (e.g., acquired imatinib tyrosine kinase inhibitor resistance), gene analysis, variants in the kinase domain
81201	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; full gene sequence
81202	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; known familial variants
81203	APC (adenomatous polyposis coli) (eg, familial adenomatosis polyposis [FAP], attenuated FAP) gene analysis; duplication/deletion variants
81206	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative
81207	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; minor breakpoint, qualitative or quantitative
81208	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis; other breakpoint, qualitative or quantitative
81210	BRAF (B-Raf proto-oncogene, serine/threonine kinase) (eg, colon cancer, melanoma), gene analysis, V600 variant(s)
81212	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; 185delAG, 5385insC, 6174delT variants

81215	BRCA1 (BRCA1, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81216	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; full sequence analysis
81217	BRCA2 (BRCA2, DNA repair associated) (eg, hereditary breast and ovarian cancer) gene analysis; known familial variant
81218	CEBPA (CCAAT/enhancer binding protein [C/EBP], alpha) (e.g., acute myeloid leukemia), gene analysis, full gene sequence
81219	CALR (calreticulin) (eg, myeloproliferative disorders), gene analysis, common variants in exon 9
81235	EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
81245	FLT3 (fms-related tyrosine kinase 3)
81246	FLT3 (fms-related tyrosine kinase 3) (eg, acute myeloid leukemia), gene analysis; tyrosine kinase domain (TKD) variants (eg, D835, I836)
81261	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); amplified methodology (eg, polymerase chain reaction)
81262	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemias and lymphomas, B-cell), gene rearrangement analysis to detect abnormal clonal population(s); direct probe methodology (eg, Southern blot)
81263	IGH@ (Immunoglobulin heavy chain locus) (eg, leukemia and lymphoma, B-cell), variable region somatic mutation analysis
81270	JAK2 (Janus kinase 2) (eg, myeloproliferative disorder) gene analysis, p.Val617Phe (V617F) variant
81273	KIT (v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog) (eg, mastocytosis), gene analysis, D816 variant(s)
81275	KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (e.g., carcinoma) gene analysis, variants in codons 12 and 13
81276	KRAS (Kirsten rat sarcoma viral oncogene homolog) (e.g., carcinoma) gene analysis; additional variant(s) (e.g., codon 61, codon 146)
81292	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81297	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81300	MSH6 (mutS homolog 6 [E. coli]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81307	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; full gene sequence
81308	PALB2 (partner and localizer of BRCA2) (eg, breast and pancreatic cancer) gene analysis; known familial variant

81301	Microsatellite instability analysis (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) of markers for mismatch repair deficiency (eg, BAT25, BAT26), includes comparison of neoplastic and normal tissue, if performed
81305	MYD88 (myeloid differentiation primary response 88) (eg, Waldenstrom's macroglobulinemia, lymphoplasmacytic leukemia) gene analysis, p.Leu265Pro (L265P) variant
81311	NRAS (neuroblastoma RAS viral [v-ras] oncogene homolog) (e.g., colorectal carcinoma), gene analysis, variants in exon 2 (e.g., codons 12 and 13) and exon 3 (e.g., codon 61)
81315	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; common breakpoints (eg, intron 3 and intron 6), qualitative or quantitative
81316	PML/RARalpha, (t(15;17)), (promyelocytic leukemia/retinoic acid receptor alpha) (eg, promyelocytic leukemia) translocation analysis; single breakpoint (eg, intron 3, intron 6 or exon 6), qualitative or quantitative
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81321	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; full sequence analysis
81322	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; known familial variant
81323	PTEN (phosphatase and tensin homolog) (eg, Cowden syndrome, PTEN hamartoma tumor syndrome) gene analysis; duplication/deletion variant
81338	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; common variants (eg, W515A, W515K, W515L, W515R)
81339	MPL (MPL proto-oncogene, thrombopoietin receptor) (eg, myeloproliferative disorder) gene analysis; sequence analysis, exon 10
81351	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; full gene sequence
81352	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; targeted sequence analysis (eg, 4 oncology)
81353	TP53 (tumor protein 53) (eg, Li-Fraumeni syndrome) gene analysis; known familial variant
81401	Molecular pathology procedure, Level 2 – MUTYH, CBFB/MYH11, EML4/ALK
81403	Molecular pathology procedure, Level 4, targeted sequence analysis – EPCAM, *VHL*
81404	Molecular pathology procedure, Level 5, targeted sequence analysis - KIR, STK11, MEN1
81405	Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis) - STK11, RET, SMAD4
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) - CDH1, MUTYH

81408	Molecular pathology procedure, Level 9 (eg, analysis of >50 exons in a single gene by DNA sequence analysis) - ATM
81432	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); genomic sequence analysis panel, must include sequencing of at least 14 genes, including ATM, BRCA1, BRCA2, BRIP1, CDH1, MLH1, MSH2, MSH6, NBN, PALB2, PTEN, RAD51C, STK11, and TP53
81433	Hereditary breast cancer-related disorders (e.g., hereditary breast cancer, hereditary ovarian cancer, hereditary endometrial cancer); duplication/deletion analysis panel, must include analyses for BRCA1, BRCA2, MLH1, MSH2, and STK11
81435	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include sequencing of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11
81436	Hereditary colon cancer syndromes (eg, Lynch syndrome, familial adenomatosis polyposis); duplication/deletion gene analysis panel, must include analysis of at least 8 genes, including APC, MLH1, MSH2, MSH6, PMS2, EPCAM, CHEK2, and MUTYH
81437	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); genomic sequence analysis panel, must include sequencing of at least 6 genes, including MAX, SDHB, SDHC, SDHD, TMEM127, and VHL
81438	Hereditary neuroendocrine tumor disorders (eg, medullary thyroid carcinoma, parathyroid carcinoma, malignant pheochromocytoma or paraganglioma); duplication/deletion analysis panel, must include analyses for SDHB, SDHC, SDHD, and VHL
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
81479	Unlisted molecular pathology procedure - RB1 GENE, ProMark
81518	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 11 genes (7 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithms reported as percentage risk for metastatic recurrence and likelihood of benefit from extended endocrine therapy – Breast Cancer Index
81519	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score
81521	Oncology (breast), mRNA, microarray gene expression profiling of 70 content genes and 465 housekeeping genes, utilizing fresh frozen or formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk of distant metastasis (Can be used for MammaPrint)
81522	Oncology (breast), mRNA, gene expression profiling by RT-PCR of 12 genes (8 content and 4 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence risk score (EndoPredict)

81523	Oncology (breast), mRNA, next-generation sequencing gene expression profiling of 70 content genes and 31 housekeeping genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as index related to risk to distant metastasis (MammaPrint)
81541	Oncology (prostate), mRNA gene expression profiling by real-time RT-PCR of 46 genes (31 content and 15 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a disease-specific mortality risk score
81542	Oncology (prostate), mRNA, microarray gene expression profiling of 22 content genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as metastasis risk score
81546	Oncology (thyroid), mRNA, gene expression analysis of 10,196 genes, utilizing fine needle aspirate, algorithm reported as a categorical result (eg, benign or suspicious) (Afirma)
81599	Unlisted multianalyte assay with algorithmic analysis (PathfinderTG)
86386	Nuclear Matrix Protein 22 (NMP22), qualitative – May also be addressed by Avalon Lab Management
0005U	Oncology (prostate) gene expression profile by real-time RT-PCR of 3 genes (ERG, PCA3, and SPDEF), urine, algorithm reported as risk score - ExosomeDx® Prostate (IntelliScore)
0016U	Oncology (hematolymphoid neoplasia), RNA, BCR/ABL1 major and minor breakpoint fusion transcripts, quantitative PCR amplification, blood or bone marrow, report of fusion not detected or detected with quantitation
0026U	Oncology (thyroid), DNA and mRNA of 112 genes, next-generation sequencing, fine needle aspirate of thyroid nodule, algorithmic analysis reported as a categorical result ("Positive, high probability of malignancy" or "Negative, low probability of malignancy") (Thyroseq)
0037U	Targeted genomic sequence analysis, solid organ neoplasm, DNA analysis of 324 genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden (FoundationOne CDx™ (F1CDx))
0040U	BCR/ABL1 (t(9;22)) (eg, chronic myelogenous leukemia) translocation analysis, major breakpoint, quantitative - MRDx BCR-ABL Test
0047U	Oncology (prostate), mRNA, gene expression profiling by real-time RT-PCR of 17 genes (12 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as a risk score - Oncotype DX Genomic Prostate Score
0239U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free DNA, analysis of 311 or more genes, interrogation for sequence variants, including substitutions, insertions, deletions, select rearrangements, and copy number variations (FoundationOne® Liquid CDx, Foundation Medicine, Inc, Foundation Medicine, Inc)
0242U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 55-74 genes, interrogation for sequence variants, gene copy number amplifications, and gene rearrangements – Guardant360 CDx
0287U	Oncology (thyroid), DNA and mRNA, next-generation sequencing analysis of 112 genes, fine needle aspirate or formalin-fixed paraffin-embedded (FFPE) tissue, algorithmic prediction of cancer recurrence, reported as a categorical risk result (low, intermediate, high) - ThyroSeq® CRC
0326U	Targeted genomic sequence analysis panel, solid organ neoplasm, cell-free circulating DNA analysis of 83 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden - Guardant360®

0334U	Oncology (solid organ), targeted genomic sequence analysis, formalin-fixed paraffin-embedded (FFPE) tumor tissue, DNA analysis, 84 or more genes, interrogation for sequence variants, gene copy number amplifications, gene rearrangements, microsatellite instability and tumor mutational burden (Guardant360 TissueNext™)
0340U	Oncology (pan-cancer), analysis of minimal residual disease (MRD) from plasma, with assays personalized to each patient based on prior next-generation sequencing of the patient's tumor and germline DNA, reported as absence or presence of MRD, with disease-burden correlation, if appropriate - Signatera
0364U	Oncology (hematolymphoid neoplasm), genomic sequence analysis using multiplex (PCR) and next-generation sequencing with algorithm, quantification of dominant clonal sequence(s), reported as presence or absence of minimal residual disease (MRD) with quantitation of disease burden, when appropriate - ClonoSEQ
0422U	Oncology (pan-solid tumor), analysis of DNA biomarker response to anti-cancer therapy using cell-free circulating DNA, biomarker comparison to a previous baseline pre-treatment cell-free circulating DNA analysis using next-generation sequencing, algorithm reported as a quantitative change from baseline, including specific alterations, if appropriate (Guardant360 Response™)

Considered Not Medically Necessary:

Coding	Description
81120	IDH1 (isocitrate dehydrogenase 1 [NADP+], soluble) (eg, glioma), common variants (eg, R132H, R132C)
81121	IDH2 (isocitrate dehydrogenase 2 [NADP+], mitochondrial) (eg, glioma), common variants (eg, R140W, R172M)
81264	IGK@ (Immunoglobulin kappa light chain locus) (eg, leukemia and lymphoma, B-cell), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81309	PIK3CA (phosphatidylinositol-4, 5-biphosphate 3-kinase, catalytic subunit alpha) (eg, colorectal and breast cancer) gene analysis, targeted sequence analysis (eg, exons 7, 9, 20)
81314	PDGFRA (platelet-derived growth factor receptor, alpha polypeptide) (e.g., gastrointestinal stromal tumor [GIST]), gene analysis, targeted sequence analysis (e.g., exons 12, 18)
81327	SEPT9 (Septin9) (eg, colorectal cancer) promoter methylation analysis
81340	TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using amplification methodology (eg, polymerase chain reaction)
81341	TRB@ (T cell antigen receptor, beta) (eg, leukemia and lymphoma), gene rearrangement analysis to detect abnormal clonal population(s); using direct probe methodology (eg, Southern blot)
81342	TRG@ (T cell antigen receptor, gamma) (eg, leukemia and lymphoma), gene rearrangement analysis, evaluation to detect abnormal clonal population(s)
81345	TERT (telomerase reverse transcriptase) (eg, thyroid carcinoma, glioblastoma multiforme) gene analysis, targeted sequence analysis (eg, promoter region
81402	Molecular pathology procedure, Level 3, gene rearrangement analysis, evaluation to detect abnormal clonal population
81449	Targeted genomic sequence analysis panel, solid organ neoplasm, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, MET, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed; RNA analysis

81456	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm or disorder, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MET, MLL, NOTCH1, NPM1, NRAS, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, or isoform expression or mRNA expression levels, if performed; RNA analysis
81552	Oncology (uveal melanoma), mRNA, gene expression profiling by real-time RT-PCR of 15 genes (12 content and 3 housekeeping), utilizing fine needle aspirate or formalin-fixed paraffin-embedded tissue, algorithm reported as risk of metastasis
0018U	Oncology (thyroid), microRNA profiling by RT-PCR of 10 microRNA sequences, utilizing fine needle aspirate, algorithm reported as a positive or negative result for moderate to high risk of malignancy (ThyraMIR™)
0045U	Oncology (breast ductal carcinoma in situ), mRNA, gene expression profiling by real-time RT-PCR of 12 genes (7 content and 5 housekeeping), utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score (The Oncotype DX® Breast DCIS Score™ TesT)
0069U	Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score (miR-**31***now*™, GoPath Laboratories)
0080U	Oncology (lung), mass spectrometric analysis of galectin-3-binding protein and scavenger receptor cysteine-rich type 1 protein M130, with five clinical risk factors (age, smoking status, nodule diameter, nodule-spiculation status and nodule location), utilizing plasma, algorithm reported as a categorical probability of malignancy (BDX-**XL2**, Biodesix®)
0089U	Oncology (melanoma), gene expression profiling by RTqPCR, PRAME and LINC00518, superficial collection using adhesive patch(es) (Pigmented Lesion Assay (PLA), DermTech)
0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) (CustomNext + RNA: *MLH1)*
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) (CustomNext + RNA: *MSH2)*
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) (CustomNext + RNA: MSH6)
0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) (CustomNext + RNA: PMS2)
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure) CustomNext + RNA: Lynch (MLH1, MSH2, MSH6, PMS2)
0244U	Oncology (solid organ), DNA, comprehensive genomic profiling, 257 genes, interrogation for single-nucleotide variants, insertions/deletions, copy number alterations, gene rearrangements, tumor-mutational burden and microsatellite instability, utilizing formalin-fixed paraffin-embedded tumor tissue (Oncotype MAPTM Pan-Cancer Tissue Test)
0250U	Oncology (solid organ neoplasm), targeted genomic sequence DNA analysis of 505 genes, interrogation for somatic alterations (SNVs [single nucleotide variant], small insertions and deletions, one amplification, and four translocations), microsatellite instability and tumor-mutation burden (PGDx elio^{TM} tissue complete)
0261U	Oncology (colorectal cancer), image analysis with artificial intelligence assessment of 4 histologic and immunohistochemical features (CD3 and CD8 within tumor-stroma border and tumor core), tissue, reported as immune response and recurrence-risk score (Immunoscore®)

0288U	Oncology (lung), mRNA, quantitative PCR analysis of 11 genes (BAG1, BRCA1, CDC6, CDK2AP1, ERBB3, FUT3, IL11, LCK, RND3, SH3BGR, WNT3A) and 3 reference genes (ESD, TBP, YAP1), formalin-fixed paraffin-embedded (FFPE) tumor tissue, algorithmic interpretation reported as a recurrence risk score (DetermaRx™)
0317U	Oncology (lung cancer), four-probe FISH (3q29, 3p22.1, 10q22.3, 10cen) assay, whole blood, predictive algorithm-generated evaluation reported as decreased or increased risk for lung cancer (LungLB®)
0329U	Oncology (neoplasia), exome and transcriptome sequence analysis for sequence variants, gene copy number amplifications and deletions, gene rearrangements, microsatellite instability and tumor mutational burden utilizing DNA and RNA from tumor with DNA from normal blood or saliva for subtraction, report of clinically significant mutation(s) with therapy associations (Oncomap™ ExTra)
0342U	Oncology (pancreatic cancer), multiplex immunoassay of C5, C4, cystatin C, factor B, osteoprotegerin (OPG), gelsolin, IGFBP3, CA125 and multiplex electrochemiluminescent immunoassay (ECLIA) for CA19-9, serum, diagnostic algorithm reported qualitatively as positive, negative, or borderline (IMMray® PanCan-d)

Document History:

Revised Dates:

- 2024: May
- 2023: December
- 2023: September
- 2023: July
- 2023: February
- 2023: January
- 2022: December
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- 2022: October
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- 2012: October
- 2012: September
- 2012: July
- 2012: June
- 2012: March
- 2012: February
- 2011: December
- 2011: October
- 2011: September
- 2011: July
- 2011: June
- 2011: April
- 2011: March
- 2010: December
- 2010: July
- 2009: June
- 2009: April

Reviewed Dates:

- 2021: April
- 2019: October
- 2016: February
- 2015: February
- 2014: February
- 2010: November

Effective Date:

- February 2009

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Special Notes: *

Medical policies can be highly technical and complex and are provided here for informational purposes. These medical policies are intended for use by health care professionals. The medical policies do not constitute medical advice or medical care. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Sentara Health Plan members should discuss the information in the medical policies with their treating health care professionals. Medical technology is constantly evolving, and these medical policies are subject to change without notice, although Sentara Health Plan will notify providers as required in advance of changes that could have a negative impact on benefits.

Services mean both medical and behavioral health (mental health) services and supplies unless We specifically tell You otherwise. We do not cover any services that are not listed in the Covered Services section unless required to be covered under state or federal laws and regulations. We do not cover any services that are not Medically Necessary. We sometimes give examples of specific services that are not covered but that does not mean that other similar services are covered. Some services are covered only if We authorize them. When We say You or Your We mean You and any of Your family members covered under the Plan. Call Member Services if You have questions.

Keywords:

Acute myeloid leukemia, ALK, Analysis, autosomal recessive, BART, BCI, BCR-ABL mutation analysis, Bladder Tumor Marker, BMPR1A, Bone marrow, BRAF, BRCA1, BRCA2, BRCA, Breast cancer, Breast Cancer Index, CALR, Calreticulin Exon 9, cancer prevention, CBFB/MHY 11, CDH1, CEBPA, ClonoSEQ, Colaris, Colorectal cancer, CSF3R, Decipher, EGFR, Endopredict, Epidermal growth factor receptor, Familial Adenomatous Polyposis (FAP), FLDV, FLT3, gene mutation, gene, genetic test, Guardant 360, Guardant360 CDx, Hardy Zuckerman, HER2, Hereditary retinoblastoma, hereditary, IGH, Immuno Globulin Heavy Chain, JAK2, Juvenile polyposis syndrome, KIT Test, KRAS, Lymphoplasmacytic, Lynch syndrome, Macroglobulinemia, malignant diseases, MammaPrint, MAP, Medullary Thyroid Cancer, MEN1, MEN2, metaplastic, Multiple Endocrine Neoplasia, Mutation Analysis, MYD88, Myeloproliferative Leukemia, MYH-associated polyposis, NMP-22, NPM1, NRAS, Oncotype DX, Ovarian cancer, Pancreatic cancer, Pathfinder TG, PML/RAR Alpha, Prolaris, ProMark, Prostate, PSA, RB1, RET, Signatera, SMAD4, STK11, TP53, UroVysion, VHL, Von Hippel-Lindau syndrome, X-linked recessive,