To all beneficiaries enrolled in a Prepaid Health Plan (PHP): for questions about benefits and services available on or after implementation, please contact your PHP.

Table of Contents

Related Clinical Coverage Policies
Refer to https://medicaid.ncdhhs.gov/ for the related coverage policies listed below:
1S-9 Genetic Testing for Diagnosis and Treatment
1S-10 Genetic Testing for Carrier and Prenatal
1S-12 Genetic Testing – Next Generation Sequencing (NGS)
11B-2 Heart (Cardiac) Transplantation

1.0 Description of the Procedure, Product, or Service

Gene expression refers to the mechanism through which the genetic information stored in a gene is transformed into a functional outcome. This predominantly transpires by transcribing RNA molecules that encode proteins or non-coding RNA molecules with alternative roles. Gene expression can be likened to an "on off switch," determining the timing and location of RNA molecules and proteins production, and a "volume control," dictating the quantity of these products generated. The process of gene expression is meticulously regulated and undergoes significant changes based on various conditions and cell types. Numerous RNA and protein products derived from genes play a role in governing the expression of other genes. The extent, timing, and manner in which a gene is expressed can be evaluated by assessing the functional activity of its product or observing the phenotype associated with the gene.

1.1 Definitions

1.1.1 Adjuvant Therapy

Adjuvant therapy refers to an additional treatment approach employed after the primary treatment (such as surgery or radiation therapy) for a specific condition, typically cancer. It is administered with the intention of eliminating any remaining cancer cells that may not have been removed by the primary treatment or to reduce the risk of cancer recurrence. Adjuvant therapy aims to improve long-term outcomes and enhance the chances of cure or disease control. It is often used in conjunction with the primary treatment to provide a comprehensive and more effective approach to managing the condition.

1.1.2 Estrogen Receptor (ER)

Estrogen receptor (ER) is a protein that responds to estrogen and influences cell growth and gene expression. It is relevant in cancer treatment decisions and hormone therapies.

1.1.3 Genetics

Genetics involve investigating the impact of genes on an individual's characteristics and traits.

1.1.4 Genetic Counselor

Genetic counselors are health professionals with specialized education, training, and experience in medical genetics and counseling. They are certified by the American Board of Genetic Counseling or have an Active Candidate Status for certification. They help a beneficiary understand and adapt to the implications of genetic contributions to disease.

1.1.5 Genetic Counseling

Genetic counseling is a process of communication that allows beneficiaries and their families to make informed medical decisions. These services include obtaining a structured family medical and genetic history, constructing a multiple-generation genetic pedigree, performing an analysis of available medical information for genetic risk assessment, and counseling the beneficiary and family. This counseling includes natural history of disease, recurrence risk to family members, and availability of testing, screening and monitoring options. (Refer to **Subsection 6.2**)

A licensed provider may provide genetic counseling when there is no access to a fellowship-trained genetic subspecialty physician or a certified genetic counselor. Similar to other genetic counselors, the licensed provider shall discuss and document in the beneficiary's health record the following:

a. Likelihood of developing disease;
b. Impact of the disease;
c. Possibility of modification of either the impact or likelihood of disease;
d. Anticipated future developments in diagnosis or treatment; and
e. Informed consent to testing was obtained after the beneficiary verbalized understanding of the testing procedure, the benefits and limitations of the test, and the possible consequences of the test results.

1.1.6 Genomics

Genomics is all a person's DNA. Genomics is the study of a person's genes (the genome) explores the entirety of DNA, encompassing genes, by investigating its structure, function, mapping, and evolutionary aspects.

1.1.7 Histology

Histology is the study of tissues, focusing on their microscopic structure and composition.

1.1.8 Hormonal Therapy

Hormonal therapy is a treatment that modifies hormone levels or activity to manage hormone-sensitive conditions, such as certain types of cancer.

1.1.9 Human Epidermal Growth Factor Receptor 2 (HER2)

HER2 (Human Epidermal Growth Factor Receptor 2) is a protein receptor found on certain cells, including cancer cells. It influences cell growth and is used as a biomarker in cancer diagnosis and treatment decisions.

1.1.10 Phenotype

Phenotype refers to a person's observable traits resulting from the interaction between genes and the environment.

1.1.11 Primary Cancer

Primary cancer refers to the initial site where a cancerous tumor originates within the body before it potentially spreads to other locations.

1.1.12 Progesterone Receptor (PR)

Progesterone receptor (PR) is a protein that responds to progesterone and regulates gene expression and cellular functions, particularly in the female reproductive system. It is relevant in reproductive processes and can impact hormone-based treatments.

2.0 Eligibility Requirements

2.1 Provisions

2.1.1 General

(*The term "General" found throughout this policy applies to all Medicaid policies*)

a. An eligible beneficiary shall be enrolled in the NC Medicaid Program *(Medicaid is NC Medicaid program, unless context clearly indicates otherwise*).
b. Provider(s) shall verify each Medicaid beneficiary's eligibility each time a service is rendered.
c. The Medicaid beneficiary may have service restrictions due to their eligibility category that would make them ineligible for this service.

2.1.2 Specific

(***The term "Specific" found throughout this policy only applies to this policy***)

a. Medicaid
None Apply.

2.2 Special Provisions

2.2.1 EPSDT Special Provision: Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age

a. **42 U.S.C. § 1396d(r) [1905(r) of the Social Security Act]**

Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) is a federal Medicaid requirement that requires the state Medicaid agency to cover services, products, or procedures for Medicaid beneficiary under 21 years of age **if** the service is **medically necessary health care** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem] identified through a screening examination (includes any evaluation by a physician or other licensed practitioner).

This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his or her health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

Medically necessary services will be provided in the most economic mode, as long as the treatment made available is similarly efficacious to the service requested by the beneficiary's physician, therapist, or other licensed practitioner; the determination process does not delay the delivery of the needed service; and the determination does not limit the beneficiary's right to a free choice of providers.

EPSDT does not require the state Medicaid agency to provide any service, product or procedure:

1. that is unsafe, ineffective, experimental or investigational.
2. that is not medical in nature or not generally recognized as an accepted method of medical practice or treatment.

Service limitations on scope, amount, duration, frequency, location of service, and other specific criteria described in clinical coverage policies may be exceeded or may not apply as long as the provider's documentation shows that the requested service is medically necessary "to correct or ameliorate a defect, physical or mental illness, or a condition" [health problem]; that is, provider documentation shows how the service, product, or procedure meets all EPSDT criteria, including to correct or improve or maintain the beneficiary's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

b. **EPSDT and Prior Approval Requirements**

1. If the service, product, or procedure requires prior approval, the fact that the beneficiary is under 21 years of age does **NOT** eliminate the requirement for prior approval.
2. **IMPORTANT ADDITIONAL INFORMATION** about EPSDT and prior approval is found in the *NCTracks Provider Claims and Billing Assistance Guide,* and on the EPSDT provider page. The Web addresses are specified below.

   NCTracks Provider Claims and Billing Assistance Guide: https://www.nctracks.nc.gov/content/public/providers/provider-manuals.html

   EPSDT provider page: https://medicaid.ncdhhs.gov/

3.0 When the Procedure, Product, or Service Is Covered

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

3.1 General Criteria Covered

Medicaid shall cover the procedure, product, or service related to this policy when medically necessary, and:

a. the procedure, product, or service is individualized, specific, and consistent with symptoms or confirmed diagnosis of the illness or injury under treatment, and not in excess of the beneficiary's needs;
b. the procedure, product, or service can be safely furnished, and no equally effective and more conservative or less costly treatment is available statewide; and
c. the procedure, product, or service is furnished in a manner not primarily intended for the convenience of the beneficiary, the beneficiary's caretaker, or the provider.

3.2 Specific Criteria Covered

3.2.1 Specific criteria covered by Medicaid

Medicaid shall cover Genetic Testing - Gene Expression when the beneficiary meets the following specific criteria:

a. Medicaid shall cover Gene Expression profiling with the Oncotype DX® Breast Recurrence Score, EndoPredict®, Prosigna® Breast Cancer Prognostic Gene Signature Assay, the Breast Cancer Index℠ or MammaPrint® as a method for managing the treatment of breast cancer when **ALL** of the following criteria are met:
   1. Beneficiary underwent surgery and comprehensive pathological evaluation of the specimen has been finalized;
   2. Histology is ductal, lobular, mixed, or metaplastic;
   3. Estrogen receptor positive (ER+), or progesterone receptor positive (PR+), or both;
   4. HER2 (human epidermal growth factor receptor-2) receptor negative;
   5. pN0 (node negative) or pN1mi with axillary lymph node micrometastasis less than or equal to 2 mm;
   6. T1b to T3 (tumor size greater than 0.5 cm and less than or equal to 5.0 cm);
   7. The beneficiary and their healthcare provider are contemplating the utilization of chemotherapy as a potential therapeutic approach; and
   8. No additional gene expression profiling for breast cancer has been performed on the same tumor (such as a metastatic focus) or on multiple sites when the primary tumor is multifocal;

   OR

b. Medicaid shall cover the use of gene expression profiling with the Oncotype DX Breast Recurrence Score for postmenopausal individuals with one (1) to three (3) positive lymph nodes (pN1a, pN1b or pN1c) when the criteria in **Subsection 3.2.1(a)(1-4; 6-8)** are also met;

   OR

c. Medicaid shall cover the use of gene expression profiling with EndoPredict, Prosigna Breast Cancer Prognostic Gene Signature Assay, or the Breast Cancer Index as a genetic indicator employed to aid in determining whether to prolong adjuvant hormonal therapy beyond a five (5)-year treatment period when **ALL** of the following criteria are met:
   1. When the criteria in **Subsection 3.2.1(a)(1-6)** have been met;
   2. When the Oncotype DX Breast Recurrence Score was the initial gene expression profiling test used; and
   3. The beneficiary is a candidate for additional cancer therapy;

   OR

d. Medicaid shall cover the use of gene expression profiling with the Breast Cancer Index as a genetic indicator employed to aid in determining whether to prolong adjuvant hormonal therapy beyond a five (5)-year treatment period for beneficiaries with one(1) to three (3) positive lymph nodes (pN1a, pN1b or pN1c) when **ALL** of the following criteria are met:
   1. When the criteria in **Subsection 3.2.1(a) (1-4)** have been met;
   2. When the Oncotype DX Breast Recurrence Score was the initial gene expression profiling test used; and

3. The beneficiary is a candidate for additional hormonal or chemotherapy.

OR

e. Medicaid shall cover gene expression profiling tests for evaluation of a thyroid nodule when **ALL** of the following criteria are met:
   1. Beneficiary is age 21 years of age and older; and
   2. Thyroid nodule is indicated by **ALL** of the following:
      A. A diameter measuring one (1) cm or more on ultrasound; and
      B. Uncertain cytology (also known as cytopathology) results from an initial fine needle aspirate biopsy, as indicated by **one or more** of the following:
         i. Atypia of undetermined significance;
         ii. Follicular lesion of undetermined significance;
         iii. Follicular neoplasm;
         iv. suspicious for follicular neoplasm; or
         v. Suspicious for malignancy.

   OR

f. Medicaid shall cover gene expression profiling using AlloMap molecular expression testing to assist in identifying heart transplant recipients with stable allograft function who are at low risk for moderate or severe acute cellular rejection at the time of testing, in conjunction with standard clinical assessment when **ALL** of the following criteria are met:
   1. Beneficiary is 15 years of age or older; and
   2. At least two months (more than 55 days) post-transplant.

3.2.2 Medicaid Additional Criteria Covered

In addition to the specific criteria covered in **Subsection 3.2.1** of this policy, for **ALL** covered Gene Expression profiling tests discussed in this policy, **ALL** of the following additional criteria must be met:

a. A certified genetic counselor or ordering provider shall evaluate and counsel the beneficiary pre- and post-test. Refer to **Subsections 1.1.5** and **6.2**;
b. After genetic counseling has been provided, informed consent is obtained prior to, and beneficiary agrees to testing;
c. The test must not be duplicative of another performed test;
d. The test must be performed by a certified Clinical Laboratories Improvement Amendment (CLIA) laboratory;
e. The test must be clinically valid, based on published peer-reviewed literature, and available for the suspected diagnosis; and
f. The test must be proven scientifically valid for the identification of a specific genetically linked disease or clinical condition.

4.0 When the Procedure, Product, or Service Is Not Covered

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

4.1 General Criteria Not Covered

Medicaid shall not cover the procedure, product, or service related to this policy when:

a. the beneficiary does not meet the eligibility requirements listed in **Section 2.0;**
b. the beneficiary does not meet the criteria listed in **Section 3.0;**
c. the procedure, product, or service duplicates another provider's procedure, product, or service; or
d. the procedure, product, or service is experimental, investigational, or part of a clinical trial.

4.2 Specific Criteria Not Covered

4.2.1 Specific Criteria Not Covered by Medicaid

a. Medicaid shall not cover gene expression profiling tests with the Oncotype DX Breast Recurrence Score, EndoPredict, Prosigna Breast Cancer Prognostic Gene Signature Assay, the Breast Cancer Index or MammaPrint as a technique of managing the treatment of breast cancer when the criteria in **Section 3.0** have not been met, or for **ANY** of the following indications:
   1. To predict response to specific chemotherapy regimens;
   2. For a beneficiary with known metastatic cancer;
   3. Gene expression profiling as a technique of managing the treatment of Ductal Carcinoma in Situ (DCIS) (when DCIS is the sole breast cancer histology);
   4. Gene expression profiling for the same tumor (such as a metastatic focus) or from more than one (1) site when the primary tumor is multifocal;
   5. Use of gene expression profiling to determine risk in a beneficiary with primary breast cancer who meets the criteria in **Section 3.0** but who has made the decision to undergo or forego chemotherapy; or
   6. Oncotype DX Breast Recurrence Score, EndoPredict, Prosigna Breast Cancer Gene expression profiling as a technique of managing the treatment of breast cancer when a gene expression profiling test other than the Prognostic Gene Signature Assay, the Breast Cancer Index or MammaPrint is being used.

b. Medicaid shall not cover gene expression profiling tests for evaluation of a thyroid nodule when the criteria in **Section 3.2.2** are not met.

c. Medicaid shall not cover gene expression profiling using AlloMap for **ANY** of the following indications:
   1. Beneficiaries with a history of antibody-mediated rejection, as AlloMap is not designed to detect this type of rejection;
   2. Any use outside of heart transplant rejection monitoring, as AlloMap is not validated for other conditions; or
   3. When results would not impact clinical management, such as cases where a biopsy is already planned based on other risk factors.

4.2.2 Medicaid Additional Criteria Not Covered

None Apply.

5.0 Requirements for and Limitations on Coverage

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

5.1 Prior Approval

Medicaid shall not require prior approval for Gene Expression profiling tests; however, Medicaid shall require prior approval when exceeding the limitations found in **Attachment A, Section C.** Providers shall follow the Prior Approval requirements documented in **Subsection 5.2.1**.

5.2 Prior Approval Requirements

5.2.1 General

The provider(s) shall submit to the Department of Health and Human Services (DHHS) Utilization Review Contractor the following:

a. the prior approval request; and
b. all health records and any other records that support the beneficiary has met the specific criteria in **Subsection 3.2** of this policy.

5.2.2 Specific

None Apply.

5.3 Additional Limitations or Requirements

5.3.1 Testing Limitations

Refer to **Attachment A, Section C**, for testing limitations for CPT codes covered in this policy.

5.3.2 Documentation Requirements

When the provider requests additional units for the CPT Codes found in **Attachment A, Section C**, then, in addition to the prior approval requirements found in **Subsection 5.2.1**, the following supporting documentation is required to justify the request:

a. The reason for the test(s);
b. Previous related lab results;
c. How the test results contribute to improved health outcomes; **and**
d. How the test results alter the beneficiary's treatment and management.

6.0 Provider(s) Eligible to Bill for the Procedure, Product, or Service

To be eligible to bill for the procedure, product, or service related to this policy, the provider(s) shall:

a. meet Medicaid qualifications for participation;
b. have a current and signed Department of Health and Human Services (DHHS) Provider Administrative Participation Agreement; and
c. bill only for procedures, products, and services that are within the scope of their clinical practice, as defined by the appropriate licensing entity.

6.1 Provider Qualifications and Occupational Licensing Entity Regulations

None Apply.

6.2 Provider Certifications

Genetic counseling must be provided by a medical provider or genetic counselor that is certified by the American Board of Genetic Counseling or has an Active Candidate Status. A genetic counselor shall be employed by or under contract to hospitals or other entities that employ licensed physicians. Licensed physicians shall be responsible for providing on-site clinical supervision and be directly involved in the care of an NC Medicaid beneficiary for whom the counseling service is billed. The services of the Genetic Counselor are billed by the supervising physician.

Clinical laboratory services must be rendered only by medical care entities that are issued certifications that are in compliance with the Clinical Laboratories Improvement Amendment (CLIA) [Public Law 100-578, amended §353 of the Public Health Service Act (PHSA)].

7.0 Additional Requirements

Note: Refer to Subsection 2.2.1 regarding EPSDT Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age.

7.1 Compliance

Provider(s) shall comply with the following in effect at the time the service is rendered:

a. All applicable agreements, federal, state and local laws and regulations including the Health Insurance Portability and Accountability Act (HIPAA) and record retention requirements; and
b. All NC Medicaid's clinical (medical) coverage policies, guidelines, policies, provider manuals, implementation updates, and bulletins published by the Centers for Medicare and Medicaid Services (CMS), DHHS, DHHS division(s) or fiscal contractor(s).

8.0 Policy Implementation and History

Original Effective Date: October 1, 2024

History:

Date	Section or Subsection Amended	Change
10/01/2024	All Sections and Attachment(s)	CCP 1S-7 terminated, and coverage absorbed here. Added coverage for Prosigna, Breast Cancer Index, and MammaPrint. Added coverage for thyroid cancer.
10/01/2024	All Sections and Attachment(s)	Policy has an effective date of 06/01/2024 with an amended date of 10/01/2024.
02/01/2025	Attachment A, Section C	Procedure codes updated as part of the annual CPT update. Effective 01/01/2025.
01/01/2026	All Sections and Attachments	Updated policy template language and formatting
01/01/2026	Section 3.2.1	Added coverage for AlloMap.
01/01/2026	Section 4.2.1	Non-coverage criteria added for AlloMap.
01/01/2026	Attachment A, Section C	Added code for AlloMap.

Attachment A: Claims-Related Information

Provider(s) shall comply with the, *NCTracks Provider Claims and Billing Assistance Guide*, Medicaid bulletins, fee schedules, NC Medicaid's clinical coverage policies and any other relevant documents for specific coverage and reimbursement for Medicaid:

A. Claim Type

Professional (CMS-1500/837P transaction)

Institutional (UB-04/837I transaction)

Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines.

B. International Classification of Diseases and Related Health Problems, Tenth Revisions, Clinical Modification (ICD-10-CM) and Procedural Coding System (PCS)

Provider(s) shall report the ICD-10-CM and Procedural Coding System (PCS) to the highest level of specificity that supports medical necessity. Provider(s) shall use the current ICD-10 edition and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for code description, as it is no longer documented in the policy.

C. Code(s)

Provider(s) shall report the most specific billing code that accurately and completely describes the procedure, product or service provided. Provider(s) shall use the Current Procedural Terminology (CPT), Health Care Procedure Coding System (HCPCS), and UB-04 Data Specifications Manual (for a complete listing of valid revenue codes) and any subsequent editions in effect at the time of service. Provider(s) shall refer to the applicable edition for the code description, as it is no longer documented in the policy.

If no such specific CPT or HCPCS code exists, then the provider(s) shall report the procedure, product or service using the appropriate unlisted procedure or service code.

Breast Cancer

CPT Code	Unit Limitations
81518	Once each primary cancer occurrence
81519	Once each primary cancer occurrence
81520	Once each primary cancer occurrence
81521	Once each primary cancer occurrence
81522	Once each primary cancer occurrence
81523	Once each primary cancer occurrence

Thyroid Cancer

CPT Code	Unit Limitations
81546	Once each primary cancer occurrence
0018U	Once each primary cancer occurrence
0026U	Once each primary cancer occurrence
0245U	Once each primary cancer occurrence
0287U	Once each primary cancer occurrence

Transplant Rejection Monitoring

CPT Code	Unit Limitations
81595	First Year Post-Transplant: Monthly starting at 2 months post-transplant. Years 1–5 Post-Transplant: Every 3 to 6 months, depending on clinical stability. Beyond 5 Years Post-Transplant: May be used as needed based on clinical assessment.

Genetic Counseling

CPT Code	Unit Limitations
96041	3 units (1 unit = 30 minutes) 90 minutes total.

Unlisted Procedure or Service
CPT: The provider(s) shall refer to and comply with the Instructions for Use of the CPT Codebook, Unlisted Procedure or Service, and Special Report as documented in the current CPT in effect at the time of service.

HCPCS: The provider(s) shall refer to and comply with the Instructions For Use of HCPCS National Level II codes, Unlisted Procedure or Service and Special Report as documented in the current HCPCS edition in effect at the time of service.

D. Modifiers

Provider(s) shall follow applicable modifier guidelines.

E. Billing Units

Provider(s) shall report the appropriate code(s) used which determines the billing unit(s).

F. Place of Service

Inpatient, Outpatient, Office, Laboratory

G. Co-payments

For Medicaid refer to Medicaid State Plan:
https://medicaid.ncdhhs.gov/meetings-notices/medicaid-state-plan-public-notices

H. Reimbursement

Provider(s) shall bill their usual and customary charges.
For a schedule of rates, refer to: https://medicaid.ncdhhs.gov//