

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

1.0	Description of the Procedure, Product, or Service.....	1
	Human Immunodeficiency Virus Drug Resistance Testing.....	1
	Genotype Tests	1
	Phenotype Tests	1
	HLA-B*5701	1
	Viral Load.....	2
	Antiretroviral Therapy	2
	Adherence	2
	Regimen Failure.....	2
1.1	Definitions	2
2.0	Eligibility Requirements	3
2.1	Provisions.....	3
	2.1.1 General.....	3
	2.1.2 Specific	3
2.2	Special Provisions.....	3
	2.2.1 EPSDT Special Provision: Exception to Policy Limitations for a Medicaid Beneficiary under 21 Years of Age	3
3.0	When the Procedure, Product, or Service Is Covered.....	4
3.1	General Criteria Covered	4
3.2	Specific Criteria Covered.....	4
	3.2.1 Specific criteria covered by Medicaid	5
	3.2.2 Medicaid Additional Criteria Covered.....	5
4.0	When the Procedure, Product, or Service Is Not Covered.....	5
4.1	General Criteria Not Covered	5
4.2	Specific Criteria Not Covered.....	5
	4.2.1 Specific Criteria Not Covered by Medicaid.....	5
	4.2.2 Medicaid Additional Criteria Not Covered.....	6
5.0	Requirements for and Limitations on Coverage	6
5.1	Prior Approval	6
5.2	Prior Approval Requirements	6
	5.2.1 General.....	6
	5.2.2 Specific	6
5.3	Testing Requirements	6
5.4	Limitations.....	7
6.0	Provider(s) Eligible to Bill for the Procedure, Product, or Service	7
6.1	Provider Qualifications and Occupational Licensing Entity Regulations.....	7
6.2	Provider Certifications.....	7

**NC Medicaid
Genotyping and Phenotyping
For HIV Drug
Resistance Testing**

**Medicaid
Clinical Coverage Policy No: 1S-1
Amended Date: June 1, 2023**

7.0 Additional Requirements 8
 7.1 Compliance 8

8.0 Policy Implementation/Revision Information..... 9

Attachment A: Claims-Related Information 10
 A. Claim Type 10
 B. International Classification of Diseases and Related Health Problems, Tenth Revisions,
 Clinical Modification (ICD-10-CM) and Procedural Coding System (PCS) 10
 C. Code(s)..... 10
 D. Modifiers..... 11
 E. Billing Units..... 11
 F. Place of Service 11
 G. Co-payments 11
 H. Reimbursement 11
 I. Billing Guidelines 11

Related Clinical Coverage Policies

Refer to <https://medicaid.ncdhhs.gov/> for the related coverage policies listed below:

1.0 Description of the Procedure, Product, or Service

Human Immunodeficiency Virus Drug Resistance Testing

Human Immunodeficiency Virus (HIV) is a ribonucleic acid (RNA) virus characterized by a high replication rate throughout all stages of infection. There are four types of HIV: HIV-1, HIV-2, Human T-cell Lymphotropic Virus (HTLV) type 1, and HTLV type 2. In HIV-1, the reverse transcription enzyme required for replication is error prone, resulting in a high rate of mutations. Viral replication continues in the presence of selective drug(s). This is called drug resistance, and it is one of the most common reasons for failure of HIV therapy.

HIV drug resistance testing assesses the HIV strain(s) infecting an individual to determine each strain's resistance to specific antiretroviral drugs. Two methods are available for testing resistant HIV strains: genotypic and phenotypic. Both isolate the virus from the beneficiary. Genotype tests detect specific mutations in the genome of a beneficiary's viral isolate that are associated with antiretroviral resistance. Phenotype tests assess how well the beneficiary's virus grows in the presence of different concentrations of antiretroviral drugs and compares these concentrations with a viral strain used as a control.

Genotype Tests

Genotype tests look for genetic mutations that have been linked to a drug's resistance. Genotypic tests are performed by directly testing for specific mutations but will only detect the mutations in the predominant strain of virus. Resistant mutations in minor viral strains will not be detected in a genotype. Genotype testing is faster and easier to perform than phenotype testing. It can be performed at significantly lower cost and is more widely available throughout the United States. Standard genotype testing may not be able to be performed in individuals with HIV RNA less than 1000 copies/ml.

Phenotype Tests

Phenotype tests assess which drugs can stop HIV from growing in a laboratory setting. They measure a virus's ability to grow in different concentrations of antiretroviral drugs and the ability of drugs to block viral replication in cell culture. Disadvantages of phenotypic testing are considerable delay of reporting time due to the wait for culture growth, insensitivity to minor viral species, and relative expense.

HLA-B*5701

HLA-B*5701 (allele) is a genetic test done to detect hypersensitivity prior to the initiation of nucleoside reverse transcriptase inhibitors. This test is also done prior to re-initiation of nucleoside reverse transcriptase inhibitors in beneficiaries who have previously tolerated these drugs but whose HLA-B*5701 status is unknown.

Viral Load

Viral load is the amount of HIV RNA in a blood sample, reported as the number of HIV RNA copies per milliliter of blood plasma. The viral load provides information about the amount of HIV that is replicating in the blood plasma but is not indicative of the amount of HIV contained within cells. HIV RNA can be used in conjunction with other variables in predicting HIV progression and in determining how effectively antiretroviral therapy (ART) is working.

Antiretroviral Therapy

An antiretroviral drug is a substance that stops or suppresses the activity of a retrovirus such as HIV. *Antiviral* is sometimes used as an alternate term. Examples of antiretroviral drugs are zidovudine (AZT, brand name Retrovir), abacavir (ABC, brand name Ziagen), and tenofovir (TDF, brand name Viread). Antiretroviral drugs interfere with HIV replication to delay disease progression.

Adherence

Adherence is the degree to which a beneficiary exactly follows a prescribed treatment regimen. *Compliance* is an alternate term.

Regimen Failure

Regimen failure occurs when the anti-HIV medications being taken do not adequately control viral replication. Factors that may cause regimen failure including the following:

- a. Poor health before starting the treatment regimen.
- b. Poor adherence to the regimen (not taking medications exactly as instructed by a provider; missing doses).
- c. Previous HIV treatment or drug resistance.
- d. Alcohol or drug abuse.
- e. Medication side effects, medication toxicity, or interactions with other medications.
- f. Medication poorly absorbed by the body (pharmacokinetic issues).
- g. Medical conditions or illnesses other than HIV infection.

1.1 Definitions

None Apply.

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, or 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

Genotype and phenotype testing for HIV drug resistance is considered medically necessary when either process is used to assist in the selection of a new treatment regimen. A new regimen may be necessary if the beneficiary has experienced *any* of the following:

- a. virologically failed the prescribed regimen;
- b. achieved a suboptimal response after the initiation of ART (optimal response is defined as reduction of plasma HIV RNA to less than 50 copies/ml);
- c. has been found to have acute HIV infection;
- d. has been infected with HIV for less than 12 months;
- e. is initiating the first ART regimen regardless of duration of infection; or
- f. is pregnant and has detectable HIV RNA in plasma.

Genotype or phenotype testing is recommended prior to changing therapy for treatment failure. Resistance assays shall be obtained when beneficiaries have a viral load greater than 1,000 copies/ml and are still on the failing regimen.

It is recommended that testing for HLA-B*5701 be done to detect hypersensitivity prior to initiation of nucleoside reverse transcriptase inhibitors.

3.2.2 Medicaid Additional Criteria Covered

None Apply.

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

Genotype and phenotype testing for HIV drug resistance is not covered in the following circumstances.

- a. The viral load is less than 1,000 copies/ml.
- b. Combined genotype and phenotype testing for HIV drug resistance is considered investigational but could be considered medically necessary in a complex case where the physician believes both types of testing might provide additional useful information, not provided by one or the other. This will be determined on a case-by-case basis, and with medical documentation supporting why both tests are necessary.

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 genotyping and phenotyping for HIV drug resistance.

5.2 Prior Approval Requirements

5.2.1 General

None Apply.

5.2.2 Specific

None Apply.

5.3 Testing Requirements

The following are based on Medicare national coverage decisions.

- a. Viral quantification may be appropriate for prognostic use, including baseline determination, periodic monitoring, and monitoring of response to therapy.
- b. Measurement of plasma HIV RNA levels must be performed at the time of establishment of an HIV infection diagnosis. For an accurate baseline, two specimens in a 2-week period are appropriate.
- c. For prognosis including ART monitoring, regular, periodic measurements are appropriate. The frequency of viral load testing must be consistent with the most current Centers for Disease Control and Prevention (www.cdc.gov/hiv) guidelines for use of antiretroviral agents in adults and adolescents and pediatric HIV infection.
- d. Because different assays can produce apparent differences in absolute HIV copy number, plasma HIV RNA levels should be measured by the same analytical method each time testing is done if possible. A change in assay method may necessitate re-establishment of a baseline.
- e. In pregnant women, the purpose of ART is to reduce plasma HIV RNA to less than the limit of detection, for the benefit of both mother and child. Genotypic resistance testing is recommended for all pregnant women prior to initiation of therapy and for those entering pregnancy with detectable HIV RNA level while on therapy. Optimal prevention of perinatal transmission may require initiation of ART before results of resistance testing are available.
- f. In neonates, early diagnostic testing for the detection of HIV-1 infection must be done in order for treatment to be initiated as soon as possible. The optimal prophylactic regimen for newborns of women with antiretroviral resistance is unknown. Therefore, antiretroviral prophylaxis for an infant born to a woman with known or suspected drug resistance must be determined in consultation with a pediatric HIV specialist, preferably before delivery.

- g. In children (birth through age 16), antiretroviral drug resistance testing is recommended before initiating therapy in all treatment-naïve children and before changing therapy for treatment failure. Resistance assays must be obtained when beneficiaries have a viral load greater than 1,000 copies/ml and are still on the failing regimen or within four weeks of discontinuation of the regimen. Consultation with a specialist in pediatric HIV infection is recommended for interpretation of resistance assays when considering starting or changing an antiretroviral regimen in a pediatric beneficiary.

Note: Adult guidelines are usually appropriate for post-pubertal adolescents.

- h. The test must be ordered by a treating physician or other qualified treating non-physician practitioner within the scope of their license and in compliance with Medicaid requirements.
- i. Follow applicable CPT codes for HLA-B*5701 for hypersensitivity testing.

5.4 Limitations

The following are based on Medicare national coverage decisions.

- a. Coverage is limited to no more than two HIV-1 drug-resistant tissue tests (CPT codes 87903 and 87904) in a 12-month period. **Refer to Attachment A, letter C**, for the number of units for CPT codes 87903 and 87904.
- b. There are circumstances in which both a genotype and a phenotype test need to be obtained at the same time. If additional testing is needed within a 12-month period, an exception may be requested. Requests for exemptions are reviewed on an individual basis and may be requested by contacting the Department of Health and Human Services (DHHS) designee at 800-688-6696. Requests must include medical necessity documentation.

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

None Apply.

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/Revision Information

Original Effective Date: July 1, 1996

Revision Information:

Date	Section Revised	Change
6/1/2009 (eff. 7/1/2008)	Throughout	Initial promulgation of current coverage
7/1/2010	Throughout	Session Law 2009-451, Section 10.31(a) Transition of NC Health Choice Program administrative oversight from the State Health Plan to the Division of Medical Assistance (DMA) in the NC Department of Health and Human Services.
3/12/2012	Throughout	Technical changes to merge Medicaid and NCHC current coverage into one policy.
1/1/2013	Subsection 5.3 c	Deleted 5.3 c. CPT codes 83893 and 83896 are limited to no more than two in a 12-month period.
1/1/2013	Attachment A Subsection C. Billing Code (s)	Deleted CPT codes 83893, 83896, 83890, 83894, 83898, 83902, 83904 and 83912
10/01/2015	All Sections and Attachments	Updated policy template language and added ICD-10 codes to comply with federally mandated 10/1/2015 implementation where applicable.
03/15/2019	Table of Contents	Added, "To all beneficiaries enrolled in a Prepaid Health Plan (PHP): for questions about benefits and services available on or after November 1, 2019, please contact your PHP."
03/15/2019	All Sections and Attachments	Updated policy template language.
12/01/2019	Attachment A	Updated policy template language "Unless directed otherwise, Institutional Claims must be billed according to the National Uniform Billing Guidelines. All claims must comply with National Coding Guidelines".
12/01/2019	Attachment A (c)	Added CPT code 87535 and 87537
12/01/2019	Table of Contents	Updated policy template language, "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."
06/01/2023	All Sections and Attachments	Updated policy template language due to North Carolina Health Choice Program's move to Medicaid. Policy posted 6/1/2023 with an effective date of 4/1/2023.

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.

ICD-10-CM Code(s)	
B20	R75
B97.35	Z21
B97.39	

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.

CPT Code(s)	
87535	87901
87536	87903
87537	87904
87539	
87900	

Component Lab Codes listed below cannot be billed on the same date of service as CPT codes 87901, 87903, and 87904.

CPT Code(s)
87252
87253

Provider(s) shall bill applicable Revenue codes.

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.

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/>

I. Billing Guidelines

CPT 86701 or 86703 is performed initially.

CPT 86702 is performed when the results of 86701 are negative and clinical suspicion of HIV-2 exists.

CPT 86689 is performed only on samples that show repeated positive results by 86701, 86702, or 86703.

Note: The laboratory performing the test(s) shall bill for the service.