MetroPlus Health

Policy and Procedure

Title: HIV Resistance Testing	Division: Medical Management Department: Utilization Management
Approval Date: 9/1/2021	LOB: Medicaid, Medicare, HIV SNP, CHP, MetroPlus Gold, Goldcare I&II, Market Plus, Essential, HARP
Effective Date: 9/1/2021	Policy Number: UM-MP324
Review Date: 9/1/2022	Cross Reference Number:
Retired Date:	Page 1 of 7

1. POLICY DESCRIPTION:

HIV viral drug resistance is correlated with poor virological response to therapy. Given the ongoing challenge of adherence to antiretroviral therapy giving rise to acquired drug resistance, and the related phenomenon of transmitted drug resistance, HIV drug resistance testing remains a key tool to guiding individual HIV treatment plans. As such, these assays are useful in some situations, including when evaluating those naïve to antiretroviral treatment and those who are antiretroviral-experienced but failing therapy.

Genotypic and laboratory-based phenotypic resistance assays are used to assess viral strains and select treatment strategies. Genotypic (rather than phenotypic) testing is the preferred resistance testing to guide therapy; this is due to faster turn-around time, greater sensitivity for detecting mixtures of wild-type and resistant virus, and comparable predictors of virologic response to subsequent ART regimens of genotype tests. However, for patients in whom there are known or suspected complex drug-resistance mutation patterns, laboratory-based phenotypic testing may play a role in limited circumstances as it measures resistance more directly and can assess relative susceptibility and interactions among mutations. Proviral DNA genotypic assays may have a role in cases where patients have undetected or low-levels of HIV-1 RNA, i.e., those not considered to be virologically failing therapy, so the only way to determine the presence of archived mutations is to sequence the DNA from peripheral blood mononuclear cells.

A medication that services as a CCR5 co-receptor antagonist, maraviroc, is FDA-approved for HIV treatment. Phenotypic assays are used to evaluate the likely effectiveness of a CCR5 antagonist as part of a treatment regimen. A phenotypic assay for HIV-1 co-receptor usage should be performed whenever the use of a CCR5 antagonist is being considered, or possibly if treatment failure has occurred on a maraviroc regimen. HIV-1 proviral DNA phenotypic tropism tests are available for patients with low-level or undetected viremia.

2. RESPONSIBLE PARTIES:

RESPONSIBLE PARTIES: Medical Management Administration, Utilization Management, Claims Department.

3. DEFINITIONS:

Genotypic resistance assays: Detect treatment-resistant genetic mutations known to be associated with therapeutic failure by directly sequencing the genomic coding region of the protein inhibited by the ART drug. These assays generally have a

minimum HIV-1 RNA viral load requirement needed for amplification (at least 500 to 1,000 copies/mL).

Phenotypic resistance assays: Assess the viral response to ART agents by using recombinant DNA methods to measure the ability of a patient's virus to grow in the presence of a drug; they can help elucidate the impact of mutation combination and interactions on each drug under consideration.

Virtual phenotype: An older, algorithmic resistance profile based on genomic sequencing. It is not a direct measure; rather, it is a prediction based on genotypic analysis and database matching

Proviral DNA genotypic assays: A next-generation sequencing genotypic assay that analyzes HIV-1 proviral DNA within peripheral blood mononuclear cells (rather than from the circulating HIV in the plasma) and can thus provide information about previously circulating resistant viral variants that are archived within proviral DNA but missed by standard resistance tests.

Virologic failure: The inability to achieve or maintain suppression of viral replication to HIV RNA level <50 copies/mL.

Incomplete virologic response: Two consecutive plasma HIV RNA levels ≥200 copies/mL after 24 weeks on an ARV regimen in a patient who has not yet had documented virologic suppression on this regimen.

Acquired drug resistance: When a drug-resistant strain of HIV emerges while a person is on antiretroviral therapy (ART) for the treatment of HIV infection, usually in the context of poor adherence to antiretroviral therapy.

Transmitted drug resistance: When a person acquires a strain of HIV that is already resistant to certain antiretroviral (ARV) drugs.

Tropism: When HIV selectively attaches to a particular coreceptor on the surface of a host CD4 cell. HIV can attach to either the CCR5 coreceptor (R5-tropic) or the CXCR4 coreceptor (X4-tropic) or both (dual-tropic). A single antiretroviral therapy agent, maraviroc, uses the CCR5 coreceptor to enter the CD4 cells.

Tropism testing: This testing, typically only phenotypic, determines whether HIV uses the CCR5 coreceptor, the CXCR4 coreceptor, or a combination of both to enter/infect CD4+ T-cells. It is considered absolutely critical when considering the use of the CCR5 antagonist maraviroc; there may also be utility in the context of virologic failure on a CCR5 inhibitor.

Proviral DNA phenotypic tropism testing: These assays evaluate the HIV-1 proviral DNA integrated within infected cells for CCR5-, CXCR4- or both-utilizing viral strains. As such, they can be conducted when HIV RNA <1,000 copies/mL.

4. POLICY:

MetroPlus considers HIV drug resistance testing medically necessary for the following groups:

a. Antiretroviral therapy-naive persons at entry into care for persons with HIV to guide selection of the initial antiretroviral therapy (ART) regimen
b. Antiretroviral therapy-naïve persons immediately prior to initiation of antiretroviral therapy, if treatment was delayed after entry into care.
c. Antiretroviral-experienced persons on combination ART with HIV RNA levels > 1000 copies/mL on at least one occasion
d. Antiretroviral-experienced persons on combination ART with HIV RNA levels consistently > 500 copies/mL
e. Antiretroviral-experienced persons on combination ART with suboptimal viral load response
f. Anyone entering pregnancy with detectable HIV RNA levels while on antiretroviral therapy
g. Prior to alteration of ARV regimen in suppressed individuals or those with low level viremia (<500 copies/ml) without available complete resistance assay results

Resistance test selection requirements:

- MetroPlus considers a genotype the only appropriate assay for all antiretroviral therapy-naïve persons.
- For antiretroviral-experienced persons on combination ART where there are known or suspected complex drug-resistance mutation patterns, phenotypic testing will be considered medically necessary.
- In persons with antiretroviral experience and known or suspected drug-resistance mutation patterns with low HIV RNA levels (< 500 copies/ml), a proviral DNA genotypic test will be considered medically necessary.

Tropism testing requirements:

- MetroPlus considers phenotypic HIV tropism testing (e.g., Trofile) medically necessary for determining virus tropism of HIV-infected persons immediately

before commencement of a chemokine receptor 5 (CCR5) antagonist (e.g., maraviroc [Selzentry]).

- Repeat tropism testing may be medically necessary if time has elapsed since the last tropism test as long as there is no prior evidence that the virus uses CXCR4 to enter CD4+ T-cells.
- Tropism testing for any other indications (e.g., for predicting disease progression) is considered experimental and investigational.
- Phenotypic tropism testing or proviral DNA phenotypic tropism testing may be medically necessary when HIV-1 RNA is <1000 copies/mL.

5. LIMITATIONS/ EXCLUSIONS:

The following two (2) genotypic drug resistance service codes are each reimbursable maximum 3 times per calendar year: 87901, 87906. Phenotypic drug resistance testing (87903, 87904) may be reimbursable on one date of service per calendar year. The Trofile Co-receptor Tropism Assay (CPT code 87999) is reimbursable once per calendar year and is subject to retrospective review for appropriate utilization. CPT code 87900 is not reimbursable.

6. All service codes listed are covered and payable ONLY if billed with any of these three (3) ICD-10 codes: B20, Z21, O987.

6. APPLICABLE PROCEDURE CODES:

CPT	Description
87901	Infectious agent genotype analysis by nucleic acid (DNA or RNA); HIV 1, reverse transcriptase and protease
87903	Infectious agent phenotype analysis by nucleic acid (DNA or RNA) with drug resistance tissue culture analysis, HIV 1; first through 10 drugs tested
+ 87904	each additional drug tested (List separately in addition to code for primary procedure)

87906	Infectious agent genotype analysis by nucleic acid (DNA or RNA); HIV-hyphen1, other region (e.g. integrase, fusion)

7. APPLICABLE DIAGNOSIS CODES:

CODE	Description
B20	Human immunodeficiency virus [HIV] disease
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status
O98.7	Human immunodeficiency virus [HIV] disease complicating pregnancy, childbirth and the puerperium

8. REFERENCES:

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REVISION LOG:

REVISIONS	DATE
Creation date	7/1/2021
Annual Review	9/1/2022

Approved:	Date:	Approved:	Date:
Digitally signed by glendon henry Date: 2021.10.04 15:52:27 -04'00'		Sanjiv Shah MD Digitally signed by Sanjiv Shah MD Date: 2021.10.06 08:08:59 -04'00'	10.6.21
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Medical Guideline Disclaimer:

 The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, Metroplus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered andor paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members.

All coding and website links are accurate at time of publication.

MetroPlus Health Plan has adopted the herein policy in providing management, administrative and other services to our members, related to health benefit plans offered by our organization.