FEP 2.04.49 Laboratory Testing for HIV Tropism

Effective Date: April 15, 2018

Related Policies: None

Laboratory Testing for HIV Tropism

Description

HIV tropism testing can determine the predominant coreceptor protein used by HIV to infect target cells. Tropism testing can help select patients for treatment with HIV coreceptor antagonists (eg, maraviroc), which block specific coreceptor proteins.

FDA REGULATORY STATUS

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. HIV tropism tests are is available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the FDA has chosen not to require any regulatory review of this test.

The FDA-approved full prescribing information for maraviroc (Selzentry™, Pfizer) states that: "Tropism testing must be conducted with a highly sensitive and specific tropism assay that has demonstrated the ability to identify patients appropriate for [maraviroc] use."[4]

POLICY STATEMENT

HIV tropism testing (see Policy Guidelines section for testing methods) may be considered **medically necessary** for selecting patients for treatment with HIV coreceptor antagonists, such as maraviroc, when there is an immediate plan to prescribe a coreceptor antagonist.

HIV tropism testing without immediate plans to prescribe HIV coreceptor antagonists such as maraviroc is **not medically necessary**.

Repeat HIV tropism testing during coreceptor antagonist treatment or after failure with coreceptor antagonists is **investigational**.

HIV tropism testing to predict disease progression (irrespective of coreceptor antagonist treatment) is **investigational**.

POLICY GUIDELINES

Testing should be conducted immediately before intended prescribed use of maraviroc to obtain the most accurate prediction of tropism at the start of treatment.

Either phenotypic or V3 population genotypic testing may be used to determine HIV tropism; both are not necessary.

V3 population genotypic testing may be conducted by either standard V3 sequencing via Sanger methods (amplification and population sequence analysis of patient-derived V3 region) or V3 deep sequencing methods (synonyms: ultra-deep sequencing; pyrosequencing; next-generation sequencing). In the United States, the only currently commercially available plasma HIV DNA coreceptor genotypic test (requires HIV viral load of ≥1000 copies/mL) includes step-wise testing, with an initial standard sequencing with reflex to V3 deep sequencing if standard sequencing detects only CCR5-tropic virus.

Genetic Counseling

Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual's family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

BENEFIT APPLICATION

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient's existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

RATIONALE

Summary of Evidence

For individuals who have HIV infection who are being considered for HIV coreceptor antagonist therapy who receives HIV tropism testing, the evidence includes RCTs. Relevant outcomes are overall survival, disease-specific survival, morbid events, quality of life, hospitalizations, medication use, and treatment-related morbidity. RCTs on treatment-naive and treatment-experienced HIV-infected patients have provided evidence that selection of candidates for HIV coreceptor antagonist therapy using HIV tropism testing results in higher rates of treatment success compared with HIV coreceptor antagonist therapy without HIV tropism testing. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with HIV infection receiving HIV coreceptor antagonist therapy or who have failed coreceptor antagonist therapy who receives HIV tropism testing, the evidence includes post hoc analysis of RCTs and observational studies. Relevant outcomes are overall survival, disease-specific survival, morbid events, quality of life, hospitalizations, medication use, and treatment-related mortality and morbidity. Current evidence does not indicate improved outcomes with additional tropism monitoring during treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with HIV infection who are undergoing tests to predict disease progression who receive HIV tropism testing, the evidence includes observational studies. Relevant outcomes are overall survival, disease-specific survival, morbid events, quality of life, hospitalizations, and medication use. Current evidence is inconsistent in as relates to whether HIV tropism testing independently predicts disease progression among HIV-infected patients. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

HIV Medicine Association of the Infectious Disease Society of North America

The HIV Medicine Association of the Infectious Disease Society of North America updated its guidelines on the on the management of persons infected with HIV in 2013.[64] These guidelines stated that tropism testing should be performed if the use of a CCR5 antagonist is being considered (strong recommendation, high quality evidence). The guidelines also stated that "routine tropism testing is not recommended prior to initiation of other regimens because of cost and lack of demonstrated benefit." The guidelines did not specify the preferred method of tropism testing.

European Consensus Group

The European Consensus Group recommendations on clinical management of tropism testing stated that tropism testing is indicated for patients who fail treatment or have unacceptable toxicity and a CCR5 inhibitor is being considered.[40] In the absence of evidence, the group provided no guidance regarding tropism testing for newly diagnosed patients whose immediate treatment plan does not include a CCR5 inhibitor. In the absence of adequate data, the group provided no guidance on the question of testing treatment-naive patients prior to the start of a regimen not including a CCR5 inhibitor, in anticipation of the need to switch quickly to a CCR5 inhibitor due to the toxicity of the initial treatment regimen. For patients with a plasma HIV RNA load greater than 1000 copies/mL, tropism testing was recommended with the enhanced sensitivity Trofile assay or by population genotypic analysis of the V3 loop, based on a moderate level of evidence from on well-designed, nonrandomized trials or cohort studies with long-term clinical outcomes. For patients with a plasma HIV RNA load less than 1000 copies/mL, genotyping was the preferred method.

Department of Health and Human Services

The Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents published federally approved HIV and AIDS medical practice guidelines in 2014, which made the following recommendations on coreceptor tropism assays[65]:

- Recommendations with "A" (strong) rating:
  - A coreceptor tropism assay should be performed whenever the use of a CCR5 coreceptor antagonist is being considered (level of evidence: I [data from randomized controlled trials]).
  - A phenotypic tropism assay is preferred to determine HIV-1 coreceptor usage (level of evidence: I).
- Recommendations with "B" (moderate) rating:
  - Coreceptor tropism testing is also recommended for patients who exhibit virologic failure on a CCR5 antagonist (level of evidence: III [expert opinion]).
  - A genotypic tropism assay should be considered as an alternative to predict HIV-1 coreceptor usage (level of evidence: II [data from well-designed nonrandomized trials or observational studies with long-term clinical outcomes]).

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY

Date	Action	Description
December 2011	New Policy	
June 2013	Update Policy	Policy updated with literature review, new references added, Policy statement changed to read: “HIV tropism testing with either the phenotypic assay or V3 population genotyping” is medically necessary. New policy statement added: “HIV V3 deep sequencing for selecting patients for treatment with HIV co-receptor antagonists is investigational.
June 2014	Update Policy	Policy updated with literature review; References 1, 5, 22, 40, and 42 added. Rationale section reorganized. Policy statement changed to remove statement that HIV V3 genotyping by deep sequencing is investigational; statement added to Policy Guidelines that V3 genotyping may be conducted by either standard sequencing methods or deep sequencing.
June 2015	Update Policy	Policy updated with literature review. References 1, 2, 4, 21-24, 39-41, 49, 53-56, 58 added. Policy statement changed to remove criteria for MN (active viral replication) to be consistent with FDA prescribing information for maraviroc.
March 2018	Update Policy	Policy updated with literature review through December 14, 2017; references 11, 13, 47, 49, 50, 55, 60 and 61 added; notes 7 and 65 updated. Policy statements unchanged.