Protocol

Laboratory Testing for HIV Tropism

(20449)

Medical Benefit		**Effective Date**: 07/01/14	**Next Review Date**: 03/15
Preauthorization	No	**Review Dates**: 05/09, 03/10, 03/11, 03/12, 03/13, 03/14	

The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. ***Preauthorization is not required.*** *Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

Description

HIV tropism testing can determine the predominant co-receptor protein used by the human immunodeficiency virus (HIV) to infect target cells. Tropism testing can help select patients for treatment with HIV co-receptor antagonists, such as maraviroc, which block specific co-receptor proteins.

Background

HIV-1, which causes AIDS, uses coreceptor proteins (either CCR5 or CXCR4) on the surface of target cells to enter and infect the cells. The most commonly transmitted strains of HIV-1 bind to CCR5 and are said to have "tropism" for CCR5-expressing cells. Dual or mixed (D/M) tropic viruses can bind to either receptor type. It is estimated that around 85% of treatment-naïve patients harbor CCR5-tropic virus only, around 15% harbor D/M virus, and less than 1% are infected with CXCR4-tropic virus alone. CXCR4- tropic virus is associated with immunosuppression and later stages of disease. New, experimental drugs, termed coreceptor antagonists, have been designed to interfere with the interaction between HIV-1 and its co-receptors.

Maraviroc (Selzentry™, Pfizer) is the first coreceptor antagonist to be approved by the U.S. Food and Drug Administration (FDA). Maraviroc is a selective, slowly reversible, small-molecule antagonist of the interaction between human cell surface CCR5 and HIV-1 gp120, also necessary for HIV-1 cell infection. Blocking this interaction prevents CCR5-tropic HIV-1 entry into cells. However, CXCR4-tropic HIV-1 entry is not prevented. According to the label, maraviroc, in combination with other antiretroviral agents, is indicated for adult patients who:

- are treatment experienced, or
- are treatment naïve (approved as of November 24, 2009);
- are infected with only CCR5-tropic detectable HIV-1;
- have evidence of viral replication.

The FDA-approved full prescribing information for the drug 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." This is because efficacy was not demonstrated in a phase II study of maraviroc in patients with D/M or CXCR4-tropic HIV-1. Due to potential adverse effects (hepatic and cardiotoxicity), maraviroc should only be used in indicated patients.

Other HIV coreceptor antagonists are in the drug development pipeline. Cenicriviroc (Tobira Therapeutics) is a small-molecule antagonist of both CCR5 and CCR2, a receptor involved in a number of inflammatory diseases, that is currently being investigated for treatment of CCR5-tropic HIV. (1)

HIV tropism testing is available by either phenotypic or genotypic methods. Tropism testing with a phenotypic assay, a cellular-based assay that functionally determines tropism, is available with the enhanced sensitivity Trofile™ assay (Monogram Biosciences, South San Francisco, CA) assay (ESTA). This phenotypic assay uses virus stocks pseudotyped with envelope sequences derived from patient plasma to infect cell lines engineered to express CCR5 or CXCR4 HIV-2 coreceptors. Genotypic tropism testing is based on sequencing the third variable (V3) loop of the HIV glycoprotein 120 gene, because the V3 loop interacts with the HIV coreceptor, and mutations in V3 are associated with measurable changes in HIV tropism. Tropism assignment is derived from the sequence data using a bioinformatic algorithm such as geno2pheno. In the U.S., the only commercially available genotypic HIV coreceptor tropism assay is available from Quest Diagnostics.

Policy (Formerly Corporate Medical Guideline)

HIV tropism testing (see Policy Guidelines for testing methods) may be considered **medically necessary** for selecting patients for treatment with HIV co-receptor antagonists such as maraviroc when there is an immediate plan to prescribe a co-receptor antagonist. Patients indicated for testing:

- have evidence of viral replication, and
- have failed multiple antiretroviral treatment regimens, or
- are treatment naïve.

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

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

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

Policy Guideline

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 U.S., the only currently commercially available plasma HIV DNA coreceptor genotypic test (requires HIV viral load of 1000 copies/mL or more) includes step-wise testing, with an initial standard sequencing with reflex to V3 deep sequencing if standard sequencing detects only CCR5-tropic virus.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to

conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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