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 HIV virus 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.

The human immunodeficiency virus (HIV-1), which causes acquired immunodeficiency syndrome, uses co-receptor 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 co-receptor antagonists, have been designed to interfere with the interaction between HIV-1 and its co-receptors.

Maraviroc (Selzentry™, Pfizer) is the first co-receptor 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.

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™ (Monogram Biosciences, South San Francisco, CA) assay. 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 co-receptors. Other phenotypic assays have been developed (e.g., in Europe) but commercial availability in the United States is uncertain. Genotypic tropism testing, which infers tropism on the basis of sequencing data, was first available with the SensiTrop assay. However, the SensiTrop assay has been discontinued and replaced by assays from other commercial and laboratory sources. For example, Quest Diagnostics Inc. offers the HIV-1 Coreceptor Tropism test, which is based on heteroduplex analysis of PCR-amplified and sequenced regions of the HIV-1 envelope V3 loop.

Corporate Medical Guideline

HIV tropism testing with either the phenotypic assay or V3 population genotyping (see Policy Guidelines) may be considered medically necessary for selecting patients for treatment with HIV co-receptor antagonists such as maraviroc. Patients indicated for testing:

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

HIV V3 deep sequencing (synonyms: ultra-deep sequencing; pyrosequencing; next generation sequencing) for selecting patients for treatment with HIV co-receptor antagonists is considered investigational.

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 prior to 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.

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.


