

## **Drug Therapy Guidelines: Selzentry® (Maraviroc)**

*Effective Date: 5/1/08*

*Committee Review Date: 11/27/07, 3/25/08*

### **Policy Statements:**

**Non-Formulary or Prior Authorization drugs will require an appropriate trial of a Formulary agent(s) based on clinical criteria. Members with a closed Formulary (2 Tier) prescription benefit are limited to use of Formulary agents only. A therapeutic trial of samples of a Non-Formulary or Prior Authorization agent will not be accepted as appropriate.**

**Please be sure to list all therapies that have been previously tried on the request form so that your request can be processed in a timely manner.**

### **What it Does and How it is Used:**

- In 2005, human immunodeficiency virus (HIV) infected approximately 40,000 Americans and over 16,000 people with acquired immunodeficiency syndrome (AIDS) died. More than 1 million people who are infected with HIV continue to live in the U.S. and may require antiretroviral therapy.
- HIV is transmitted via bodily fluids, making unprotected sexual intercourse, contaminated needles, and nursing/childbirth from an infected mother all common routes of transference.
- Infection is usually followed by a progressive decrease of the CD4+ T cell (a type of white blood cell) count and an increase in viral load.
- The latency period of the infection can last anywhere from two weeks to 20 years.
- HIV progresses to AIDS when the CD4+ T cell levels drop below a critical level. Cell-mediated immunity is compromised and opportunistic infections begin to materialize, resulting in recurring respiratory tract infections, skin rashes, oral ulcerations, and an increased susceptibility to oral candidiasis.
- The goal of drug therapy is to delay the progression of HIV to AIDS and the current standard of care for HIV patients includes a highly active antiretroviral therapy (HAART) regimen, which generally consists of at least 3 drugs from two different classes of antiretroviral agents [usually 2 nucleoside analogue reverse transcriptase inhibitors (NRTIs) and either a non-nucleoside reverse transcriptase inhibitor (NNRTI) or protease inhibitor(PI)]
- HIV uses several different cell receptors and at least 1 of 2 different co-receptors called CXCR4 and CCR5 to enter and infect cells.
- HIV can then be stratified into 3 different categories; HIV that prefers using CXCR4 (CXCR4 tropic), CCR5 (CCR5 tropic) or either co-receptor (dual- or mixed-tropic).
- Maraviroc (Selzentry®) is a CCR5 co-receptor antagonist indicated for combination antiretroviral treatment of treatment-experienced adults infected with only CCR5-tropic HIV-1, who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents.

- Maraviroc (Selzentry®) works by blocking the binding of HIV-1 gp120 to the CCR5 co-receptor in a selective and slowly reversible manner, which prevents HIV-1 entry into cells.
- Approval was based on two ongoing, double-blind, randomized, placebo-controlled, multicenter clinical trials called MOTIVATE-1 and MOTIVATE-2 in which patients had >5,000 copies/mL of HIV-1 RNA to be eligible for study entry. After 24 weeks of optimized background therapy plus maraviroc or placebo, the proportion of subjects with HIV-1 RNA <400 copies/mL receiving maraviroc compared to placebo was 61% and 28%, respectively.
- CXCR4-tropic and dual-tropic HIV-1 entry is not inhibited by maraviroc (Selzentry®), hence its use is not recommended in these patient populations. The antiviral activity of maraviroc against HIV-2 has not been evaluated.
- Tropism testing and treatment history should guide the use of maraviroc (Selzentry®). Trofile™ was used in all clinical trials of CCR5 antagonists.
- The greatest risk for treatment failure on maraviroc (Selzentry®) is an increase in CXCR4-using (CXCR4-tropic or dual tropic) virus levels, which appears to be related to the inability of the pre-treatment tropism assay to detect a low level of pre-existing CXCR4-using virus (CXCR4-tropic or dual tropic), rather than a co-receptor switch from CCR5-tropic virus to CXCR4-using virus resulting from mutation in the virus.
- The Trofile™ assay is able to detect CXCR4-tropic HIV 100% of the time when it comprises at least 10% of the total viral population, and 85% of the time when the CXCR4-tropic virus comprises at least 5% of the total viral population.
- The assay requires a viral load of at least 1000 copies/mL to determine tropism. All blood samples are analyzed through a central lab and results are returned to the physician in about 14 days. The Trofile™ assay costs approximately \$1900.
- Competing CCR5 assays will be introduced to the market to offer expanded access and decreased cost. For example, Quest Diagnostics will offer the SensiTrop™ assay that detects as little as 1% CXCR4-tropic virus in a sample and has a turnaround time of less than 7 days.

**What it Costs:**

<b>Concurrent Medications</b>	<b>Dose</b>	<b>AWP/ Day</b>	<b>AWP/ Month</b>	<b>AWP/ Year</b>
CYP3A inhibitors (with or without a CYP3A inducer) including: <ul style="list-style-type: none"> <li>• protease inhibitors (except tipranavir/ritonavir)</li> <li>• delavirdine</li> <li>• ketoconazole, itraconazole, clarithromycin,</li> <li>• other strong CYP3A inhibitors (e.g., nefazadone and telithromycin)</li> </ul>	150 mg twice daily	\$36	\$1,080	\$13,140
NRTIs, tipranavir/ritonavir, nevirapine, and other drugs that are not strong CYP3A inhibitors or CYP3A inducers	300 mg twice daily	\$36	\$1,080	\$13,140
CYP3A inducers (without a strong CYP3A inhibitor) including: <ul style="list-style-type: none"> <li>• efavirenz</li> <li>• rifampin</li> <li>• carbamazepine, phenobarbital, and phenytoin</li> </ul>	600 mg twice daily	\$72	\$2,160	\$26,280

**Rationale for Prior Authorization:**

To provide coverage for Selzentry® in situations where the drug has shown effectiveness (i.e. in combination antiretroviral treatment in treatment-experienced adults infected with only CCR5-tropic HIV-1, who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral agents).

**Benefit Design:**

Coverage for Selzentry® is determined through prior authorization for every claim

**Prior Authorization Criteria:**

Coverage for Selzentry® is provided in accord with the following criteria:

- Patient has evidence of HIV-1 viral replication.
- Patient has previously been treated with antiretroviral therapy and has HIV-1 strains resistant to at least two antiretroviral drugs.
- Patient is infected with only CCR5-tropic HIV-1 virus based on results from a tropism assay (use in patients with CXCR4 receptor using virus or both CCR5 and CXCR4 receptor using virus is not covered).
- Patients must be receiving concurrent treatment with optimized antiretroviral therapy (ideally, treatment with at least two active antiretroviral drugs) unless there is resistance or intolerance to these drugs.

**Coverage Duration:**

Coverage is provided for 6 months at a quantity sufficient for doses up to 1200 mg per day. Coverage is renewable for 6 months in situations in which the patient is responding to treatment (for example, treatment with maraviroc (Selzentry®) is decreasing HIV-1 RNA viral load and/or the patient's CD4 count is stable).

**References:**

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2. Centers for Disease Control and Prevention. *HIV/AIDS Surveillance Report, 2005*. Vol. 17. Rev ed. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention; 2007:12, 16-17. Also available at: <http://www.cdc.gov/hiv/topics/surveillance/resources/reports/>.
3. Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. 55(21); 585-589. June 2, 2006. Available from URL: [http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5521a1.htm?s\\_cid=mm5521a1\\_e](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5521a1.htm?s_cid=mm5521a1_e) Accessed 12 Sept. 2007.
4. DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC). Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. October 10, 2006. Available from URL: <http://AIDSinfo.nih.gov> Accessed 12 Sept. 2007.
5. Maraviroc (Selzentry®). Prescribing information. Pfizer. New York: August 2007.
6. Monogram Biosciences, Inc. Patient frequently asked questions. San Francisco, CA: August 2007. Available from URL: [http://www.trofileassay.com/FAQ\\_Patient\\_Questions#Q23](http://www.trofileassay.com/FAQ_Patient_Questions#Q23) Accessed 12 Sept. 2007.