Maraviroc (Selzentry)

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Drug Summary

Maraviroc is a unique antiretroviral medication—it is an HIV entry inhibitor that selectively binds to human C-C chemokine receptor 5 (CCR5). Maraviroc is currently the only FDA-approved agent in the CCR5 antagonist class and the only antiretroviral medication that acts by blocking or inhibiting a host protein or receptor, rather than a viral target. The entry of HIV into host cells requires HIV initially binding to the CD4 receptor followed by binding to either the CCR5 receptor or the C-X-C chemokine receptor type 4 (CXCR4). The HIV type that utilizes the CCR5 coreceptor pathway is referred to as R5-tropic HIV whereas virus that enters via the CXCR4 receptor is considered X4-tropic HIV. Because maraviroc does not block X4-tropic strains from entering host cells, it is useful only in patients who exclusively have R5-tropic HIV. Accordingly, prior to prescribing maraviroc, it is necessary to evaluate the patient’s viral tropism and maraviroc should only be prescribed in patients who solely harbor R5-tropic HIV. Maraviroc is generally well tolerated and causes few long-term adverse effects or drug interactions with non-antiretroviral medications (though dose adjustment is required with some other antiretrovirals that are strong hepatic enzyme inducers or inhibitors). The main limitations of maraviroc are the need for twice-daily dosing, the requirement to perform an HIV tropism assay prior to use, and the lack of efficacy in patients who do not have pure R5-tropic HIV. In addition, maraviroc is generally reserved for salvage therapy, since the likelihood of X4-tropic HIV increases as patients develop more advanced immunosuppression. Thus, maraviroc is not an option for many treatment-experienced patients with advanced disease.

Key Clinical Trials

Maraviroc was assessed in two phase III, double-blind, randomized controlled studies, in which treatment-experienced individuals (with 3-class drug resistance, an HIV RNA level above 5,000 copies/mL, and exclusive R5-tropic HIV) were randomized to maraviroc once daily, maraviroc twice daily, or placebo, each with an optimized background regimen [MOTIVATE 1 (A4001027)] and [MOTIVATE 2 (A4001028)]. In a combined analysis of these two studies, individuals in the maraviroc arms had significantly greater rates of HIV RNA suppression and greater increases in CD4 count than those who received placebo. A trial of treatment-naïve adults with R5-tropic HIV compared maraviroc (once-daily or twice-daily) to efavirenz, each given with zidovudine-lamivudine [MERIT (A4001026)]. The once-daily maraviroc arm was discontinued due to inferior virologic suppression. The twice-daily maraviroc arm was initially found to have lower rates of HIV suppression than the efavirenz arm, but
a later re-analysis found that the response rates were similar (in this reevaluation, viral tropism was retested using a more sensitive assay and a number of subjects whose virus was not truly R5 tropic at baseline were retrospectively excluded from the analysis). Maraviroc has also been studied as part of several 2-drug combinations for simplification of therapy and overall has not shown favorable efficacy [ROCnRAL (ANRS 157)].

**Adverse Effects**

Maraviroc is generally well tolerated but can cause upper respiratory tract symptoms, diarrhea, stomach upset, insomnia, rash, or other nonspecific symptoms.

**Use In Pregnancy**

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), maraviroc is in the category of Not Recommended for Initial ART in Pregnancy.

- For additional information regarding the safety and toxicity of maraviroc in pregnancy see the HHS Perinatal Guidelines summary on Maraviroc.

**Key Drug Interactions**

For complete information on maraviroc-related drug interactions, see the Drug Interactions section in the Maraviroc (Selzentry) Prescribing Information.