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 medications 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 and MOTIVATE 2]. 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]. 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].

**Adverse Effects**

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

**Key Drug Interactions**

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