**Maraviroc (Selzentry®)**

**Class:**
Maraviroc is a CCR5 co-receptor antagonist.

**Antiviral Activity:**
Maraviroc has activity against CCR5-tropic positive HIV-1. It does not have activity against CXCR4-tropic HIV-1, dual-tropic HIV-1, or HIV-2.

**Mechanism of Action:**
Maraviroc selectively binds to the human chemokine receptor CCR5, which is present on the cell membrane. This binding prevents the interaction of HIV-1 gp 120 with CCR5-tropic HIV-1 and thereby inhibits the virus from entering the cell.

**Mechanism of Resistance:**
Maraviroc does not have activity against CXCR4-tropic HIV-1, dual-tropic HIV-1, or HIV-2. Amongst known CCR5-tropic HIV-1, amino acid residue substitutions in the V3-loop of the HIV-1 envelope glycoprotein (gp160) are necessary for the maraviroc-resistant phenotype. These primary substitutions were isolated at A19T and I26V.

There is no cross resistance to currently available antiretrovirals.

**Pharmacodynamics:**
The *in vitro* IC$_{50}$ of maraviroc ranges from 0.1 to 4.5 nM and the *in vitro* IC$_{90}$ ranges from 0.6 to 13.4 nM.

**Pharmacokinetics:**
Maraviroc is rapidly absorbed with an absolute bioavailability of 33% following a 300mg dose. The peak plasma concentrations are reached in 0.5 - 4 hours following a single dose. Maraviroc is primarily metabolized by cytochrome P450 systems, using CYP3A4 as the major enzyme. It is 76% bound to human plasma proteins and has a volume of distribution of 194L.

**Adverse Effects:**
Maraviroc is generally well tolerated with the incidence of diarrhea, nausea, headache, and fatigue similar to or less than those of placebo. The most common adverse reactions in clinical studies are upper respiratory tract infection, cough, pyrexia, rash and dizziness.

**Dosage:**
The usual adult dose is based on concomitant medications and is indicated only for treatment experienced patients.

- With potent CYP3A4 inhibitors: 150mg twice daily
- With weak or non-CYP3A4 inhibitors: 300mg twice daily
- With CYP3A4 inducers: 600mg twice daily

Maraviroc should not be given to any patient less than 16 years of age.
No dosage adjustment is necessary in renal or hepatic failure at this time.

**Drug Interactions:**
Maraviroc is neither an inhibitor or inducer of CYP enzymes; however, it is a substrate for CYP3A4 and Pgp. Therefore, the pharmacokinetics of maraviroc are modulated by inhibitors and inducers of these enzymes/transporters.

**Contraindications/Warnings/Precautions:**
Hepatotoxicity has been reported with maraviroc and requires an immediate evaluation. Because of this, caution is warranted when administering maraviroc to patients with pre-existing liver dysfunction. In addition, more cardiovascular events were observed in patients who received maraviroc than in placebo.

**Pregnancy:**
Pregnancy category B: No human data, but not teratogenic in rats or rabbits.

**Monitoring Requirements:**
Patients must receive a coreceptor tropism assay prior to the initiation of maraviroc therapy to determine their eligibility. Only experienced patients with a CCR5-tropic HIV-1 should receive maraviroc.

Monitoring liver function tests periodically is also warranted.

**Brand names/Manufacturer:**
Selzentry®
Division of Pfizer Inc.