



Therapeutic Class ReviewSM

Antivirals - maraviroc (SelzentryTM)

December 2007

New Product for Review:
Maraviroc (SelzentryTM) [Pfizer]

Dossier Provided by Manufacturer: Yes
Dossier Evaluation: 2 (missing PE model)

- 1- Dossier missing significant clinical trial(s).
- 2- Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3- Mfg. provided all relevant trials and information.

Executive Summary

HIV infection in the United States:

- Approximately 1.2 million people in the US are infected with HIV. ^[2, 14]
 - 492,000/1.2 million (41%) of those infected with HIV are on antiretroviral therapy.
 - Of those on therapy, 77,911/492,000 (16%) are on third-line (salvage) agents.
 - Among patients on salvage agents 31,164/77,911 (~40%) have a detectable viral load. About half of these patients are infected with R5 tropic virus, the target market for maraviroc (Selzentry).
 - Based on these figures, approximately 15,500/492,000 (8%) of patients on antiretroviral therapy may be candidates for maraviroc (Selzentry).
- Despite the availability of four classes of antiretroviral agents, tolerability and resistance remain issues for a significant proportion of the HIV-infected patient population. ^[3]

Maraviroc (Selzentry)

- Maraviroc (Selzentry) belongs to a new class of antiretroviral medications called CCR5 co-receptor antagonists.
 - Blocking this co-receptor prevents entry of some strains of HIV-1 into the human host cell and stops viral replication.
 - Maraviroc (Selzentry) does not work against all strains of HIV-1.
 - Testing for the CCR5 co-receptor is necessary to guide the use of maraviroc (Selzentry). ^[1]
- Maraviroc (Selzentry) is indicated for treatment-experienced patients, a specific population of HIV-1 infected patients.
 - Treatment-experienced patients have failed several antiretroviral (ARV) regimens and have resistance to multiple ARVs, which limits their treatment options.
- Maraviroc (Selzentry) is administered twice daily and must be used in combination with other antiretroviral drugs.

Evidence

- There is no reliable evidence supporting the efficacy of maraviroc (Selzentry) in treatment-experienced HIV-infected adults.
 - Evidence is based on two identical trials that compared maraviroc (Selzentry) plus optimized background antiretroviral therapy (OBT) versus placebo plus OBT.
 - Both trials experienced very high drop-out rates and many confounding variables, flaws that are typical of all trials in HIV treatment-experienced populations.
 - In addition, the discontinuation rate between the two study arms was very unbalanced, which may impart a bias in favor of maraviroc (Selzentry).
- The two studies were not designed to detect specific harms and are of short duration (based on preliminary 24 week data).
- Interpretation of safety of maraviroc (Selzentry) is confounded by the high variability in background antiretroviral therapies.
- The most common adverse effects observed with a greater frequency in patients receiving maraviroc (Selzentry) included cough, pyrexia, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain and dizziness.
- Package labeling for maraviroc (Selzentry) includes Black Box Warnings regarding the potential for hepatotoxicity and allergic reactions.
- The incidence of cardiac ischemia was higher in patients receiving maraviroc (Selzentry) than placebo (1.3% versus 0%). It is not known whether this difference is significant. Patients in the RCTs were on varying background regimens and were not stratified based on cardiac history during randomization.

Decision

Maraviroc (Selzentry) is preferred/formulary because:

- It addresses an unmet need in HIV-infected patients who have few or no remaining treatment options.
- There is a low probability of inappropriate use.

Products

Table 1: Antiviral Medications for treatment-experienced patients:

Drug Products	FDA approval ^a	Patent Expiration(s) ^b	FDA approved indications	Usual Dose/Route	Potential Off-label Uses ^c
Fusion inhibitors:					
enfuvirtide (Fuzeon®) [4]	3/2003	6/2013	Treatment of HIV-1 infection in combination with other antiretroviral medications in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.	90 mg (1 ml) subcutaneously b.i.d.	
Protease inhibitors (PIs) for treatment-experienced patients:					
darunavir (Prezista™) [5]	6/2006	12/2015	Treatment of HIV-1 infection in combination with ritonavir and other antiretroviral agents in antiretroviral treatment-experienced patients.	600 mg p.o. b.i.d. plus ritonavir 100 mg b.i.d. [with food]	
tipranavir (Aptivus®) [6]	6/2005	12/2015	Treatment of HIV-1 infection, in combination with ritonavir, in patients who are treatment-experienced and infected with HIV-1 strains resistant to more than one protease inhibitor.	500 mg p.o. b.i.d. co-administered with ritonavir 200 mg b.i.d. [with food]	
CCR5 co-receptor antagonists					
maraviroc (Selzentry™) [1]	8/2007	5/2021	Used in combination with other antiretroviral agents in treatment-experienced adult patients infected with only CCR5-tropic HIV-1 detectable disease, showing resistance to multiple agents with evidence of HIV-1 replication despite treatment.	150 to 600mg p.o. b.i.d.	Treatment-naïve patients infected with HIV
Integrase strand transfer inhibitors (INSTIs)					
raltegravir (Isentress™) [7]	10/2007	10/2012	Treatment of HIV-1 infection in combination with other antiretroviral medications in treatment-experienced patients with evidence of HIV-1 replication despite ongoing antiretroviral therapy.	400mg p.o. b.i.d.	Treatment-naïve patients infected with HIV

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Based on patents listed in Orange Book as of 11/20/07.

^c As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

References

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