

# HIV CareLink

A Newsletter for HIV/AIDS  
Primary Care Providers

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## FDA APPROVES FIRST CCR5 INHIBITOR MARAVIROC (SELZENTRY™)

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On August 6th, 2007, the FDA approved the first drug in a new class of antiretroviral agents (ARVs), the CCR5 co-receptor antagonist maraviroc. Additional information including the package insert is available online at [www.selzentry.com](http://www.selzentry.com)

### Mechanism of action

- Maraviroc binds to the CCR5 receptor on the membrane of human cells such as CD4 cells. This binding prevents the interaction of HIV-1 gp120 and human CCR5 which is necessary for entry into the cell. Maraviroc does not prevent HIV-1 entry into CXCR4-tropic or dual-tropic cells.

### Indication

- Maraviroc is indicated (in combination with other ARVs) for treatment-experienced adult HIV-infected patients
- Maraviroc is not recommended in patients who have dual/mixed tropic or CXCR4-tropic virus
- Use of maraviroc should be based on treatment history and tropism assay results

### Co-Receptor Tropism Assay (Trofile™)

- The tropism assay is available from Monogram Biosciences, Inc. (For more information go to [monogramhiv.com](http://monogramhiv.com)); anticipated cost: approximately \$1900
- Specimen collection/processing:
  - Draw whole blood into either two 5.0 mL PPT (pearl top) or two tubes containing EDTA anticoagulant (lavender top). The Trofile™ Co-Receptor Tropism Assay requires 3.0 mL of plasma (in addition to plasma required for any other tests being done at the same time).
  - Immediately centrifuge blood samples (within 2 hrs of collection) at room temperature for 10-15 minutes immediately remove from centrifuge.

- For EDTA samples: after centrifugation, immediately remove plasma from cells and transfer to a screw-cap top tube
- Immediately after centrifugation, freeze plasma samples at or below -20° C in a standard laboratory freezer
- DO NOT THAW SAMPLES AFTER FREEZING! Samples should be frozen when picked up by courier.

### Pharmacokinetics

- Maraviroc is metabolized by CYP3A (cytochrome P450 3A) or Pgp (P-glycoprotein) and its levels can be affected by drugs that inhibit or induce CYP3A or Pgp

### Dosage and Administration<sup>1</sup>

Concomitant Medications	Maraviroc Dose
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, telithromycin)</li> </ul>	150 mg po bid
Other concomitant medications, including tipranavir/ritonavir, nevirapine, all NRTIs and enfuvirtide	300 mg po bid
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 po bid

- Can be taken with or without food. If missed dose, take as soon as possible unless it is less than 6 hours before the next scheduled dose.

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## ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

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For more information,  
please visit our website:

[www.FAETC.org](http://www.FAETC.org)

To request clinical consultation, please call the  
National Clinicians' Consultation Hotline:

**1-800-933-3413**





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**Dosage Form**

- 150 mg and 300 mg tablets (store at controlled room temperature)

**Cost**

Wholesale for either strength is approximately \$870.00 per month <sup>2</sup>

**Precautions/Adverse Effects**

- Hepatotoxicity: may be preceded by a systemic allergic reaction (↑ LFTs, pruritic rash, eosinophilia, other systemic symptoms)
- Dizziness/postural hypotension
- Increased risk of cardiovascular events (MI, ischemic events)
- Immune reconstitution syndrome
- The most common adverse events reported with a higher frequency than in placebo recipients included: cough, pyrexia, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain and dizziness
- Pregnancy category B
- If renal impairment present (CrCl < 50mL/min) and patient is on concomitant CYP3A inhibitor, patients may experience increased risk of adverse effects. Renal clearance accounts for approximately 25% of total maraviroc clearance.
- Maraviroc is metabolized by the liver, concentrations are likely to be increased in patients with hepatic impairment

**Clinical Trials**

MOTIVATE-1 & MOTIVATE-2

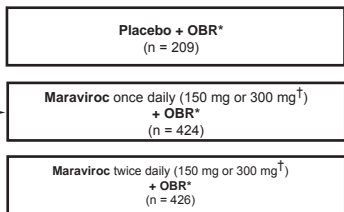
**Schematic of Study Design**

1:2:2 randomization:  
stratified by enfuvirtide use  
and HIV-1 RNA < or ≥  
100,000 copies/mL

Week 24  
planned interim analysis

Week 48

Treatment-experienced patients with CCR5-tropic HIV, HIV-1 RNA ≥ 5000 copies/mL, stable ART or no ART for ≥ 4 weeks, resistance to and/or ≥ 6 months of ≥ 1 antiretroviral from 3 classes or ≥ 2 PIs



(MOTIVATE 1: N = 601;  
MOTIVATE 2: N = 475)

ART, antiretroviral therapy.

\*Optimized background regimen comprising 3-6 antiretroviral drugs.

\*Patients receiving PI (other than tipranavir) or delavirdine received 150 mg; all others received 300 mg.

**Demographic and Baseline Characteristics of Subjects in Studies**

MOTIVATE-1 and MOTIVATE-2<sup>1</sup>

	<b>Maraviroc BID N = 426</b>	<b>Placebo N = 209</b>
Age (years) Mean (Range)	46.3 (21-73)	45.7 (29-72)
Sex		
Male	382 (89.7%)	185 (88.5%)
Female	44 (10.3%)	24 (11.5%)
Race		
White	363 (85.2%)	178 (85.2%)
Black	51 (12.0%)	26 (12.4%)
Other	12 (2.8%)	5 (2.4%)
Region		
U.S.	276 (64.8%)	135 (64.6%)
Non-U.S.	150 (35.2%)	74 (35.4%)
Subjects with Previous Enfuvirtide Use	182 (42.7%)	91 (43.5%)
Baseline Plasma HIV-1 RNA (log <sub>10</sub> copies/mL) Mean (Range)	4.85 (2.96-6.88)	4.86 (3.46-7.07)
Subjects with Screening Viral Load ≥100,000 copies/mL	179 (42.0%)	84 (40.2%)
Baseline CD4+ Cell Count (cells/mm <sup>3</sup> ) Median (Range)	167 (2-820)	171 (1-675)
Subjects with Baseline CD4+ Cell Count ≤200 cells/mm <sup>3</sup>	250 (58.7%)	118 (56.7%)
Subjects with Overall Susceptibility Score (OSS): <sup>a</sup>		
0	57 (13.4%)	35 (16.7%)
1	136 (31.9%)	44 (21.1%)
2	104 (24.4%)	59 (28.2%)
≥3	125 (29.3%)	66 (31.6%)
Subjects with enfuvirtide resistance mutations	90 (21.2%)	45 (21.5%)
Median Number of Resistance-Associated: <sup>b</sup>		
PI mutations	10	10
NNRTI mutations	1	1
NRTI mutations	6	6

a OSS -Sum of active drugs in OBT based on combined information from genotypic and phenotypic testing.

b Resistance mutations based on IAS guidelines



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## Outcomes of Randomized Treatment at Week 24

### Studies MOTIVATE-1 and MOTIVATE-2<sup>1</sup>

Outcome	Maraviroc BID N=426	Placebo N=209	Mean Difference
Mean change from Baseline to Week 24 in HIV-1 RNA (log <sub>10</sub> copies/mL)	-1.96	-0.99	0.97
<400 copies/mL at Week 24	259 (60.8%)	58 (27.8%)	33.0%
<50 copies/mL at Week 24	193 (45.3%)	48 (23.0%)	22.3%
Virologic Responders <sup>b</sup>	295 (69.2%)	75 (35.9%)	33.4%
Discontinuations			
Insufficient Clinical Response	91 (21.4%)	106 (50.7%)	
Adverse Events	16 (3.8%)	8 (3.8%)	
Other	26 (6.1%)	18 (8.6%)	
Patients with treatment-emergent CDC Category C events	18 (4.2%)	14 (6.7%)	
Deaths (during study or within 28 days of last dose)	5 (1.2%)	1 (0.5%)	

<sup>b</sup> Reduction in HIV-1 RNA  $\geq 1 \log_{10}$  or HIV-1 RNA <400 copies/mL at Week 24.

#### References:

1. Pfizer 8/2007. Package insert for Selzentry™ (maraviroc). Available at [http://media.pfizer.com/files/products/uspi\\_maraviroc.pdf](http://media.pfizer.com/files/products/uspi_maraviroc.pdf)
2. <http://aids-clinical-care.jwatch.org/cgi/content/full/2007/810/1>

### TREATING ADOLESCENTS WITH HIV:

#### Tools for Building Skills in Cultural Competence, Clinical Care and Support Larry Friedman, MD

Faculty, Florida/Caribbean AIDS Education and Training Center  
Professor and Director of Adolescent Medicine,  
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The US Department of Health and Human Services' Office of HIV/AIDS Policy within the Health Resources and Services Administration announces the launching of a new online training series for health care providers. Entitled "Treating Adolescents with HIV: Tools for Building Skills in Cultural Competence, Clinical Care and Support," the training is designed for MDs, NPs, PAs, RNs, social workers, psychologists, case managers, and other health professionals who are interested in the care of teenagers and young adults actively coping with HIV infection. The introduction reviews "best practices" in adolescent care, including the impact of HIV on minority US youth especially. The four additional modules address concepts surrounding psychosocial issues, antiretroviral treatment and adherence, transitioning care from pediatric to adult settings, and prevention practices for infected individuals. Cultural competence and sensitivity to age group are themes that are highlighted throughout this practical and educational activity.

The training modules were produced by John Snow, Inc. under subcontract to WriteProcess, Inc. The AETC National Resource Center, along with the Adolescent AIDS Program in the Bronx, NY and other nationally recognized youth HIV specialists, contributed expert information, course materials, interactive questions, and video segments. The training is easily accessible and free, offering continuing education credits for participants. For details, please see [www.hivcareforyouth.org](http://www.hivcareforyouth.org)

### The Rainbow Center for Women, Adolescents, Children and Families

at the College of Medicine Jacksonville Department of Pediatrics

Presents



### The 11th Annual Infectious Diseases and HIV/AIDS Conference of Northeast Florida

October 18 – 19, 2007

The Jacksonville Marriott  
Jacksonville, Florida

Brochure at <http://www.FAETC.org/NEFL>

Register at <http://cme.ufl.edu>

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