Risk Management Program

Data Source	Start	Contribution to Safety Knowledge
Pharmacovigilance	3Q07	Post-marketing surveillance of spontaneous SAE reports
Phase 2b/3 TN Study (1026)	2Q05	Follow-up until LSLV: 5 years
Phase 2b/3 TE Study (1027/1028)	4Q04	Follow-up until LSLV: 96 weeks 5 year follow-up for mortality
Expanded access program	2Q07	Overall safety in broader patient population
Safety registry	4Q07	Real-world use: Category C events; malignancies; MI; liver failure; mortality
EuroSIDA and other HIV cohort collaborations	1Q07	Provide HIV general population event rates
Automated database study	TBD	Real-world use: major safety endpoints
Pediatric studies	4Q07	Safety and efficacy in children
In utero exposure: with cohorts and antiretroviral pregnancy registry	TBD	Potential effects of *in utero* exposure to maraviroc

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Conclusions and Dose Recommendations

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Overall Conclusions

Based on data from adequate and well-controlled clinical trials with 6-12 months of follow-up in treatment experienced patients infected with R5-tropic virus:

- Maraviroc is effective in reducing viral load and increasing CD4 count in all treatment subgroups
- Maraviroc is well tolerated
  - With little evidence of postural hypotension
    - Although a slight excess of ischemic adverse events was noted
  - Without evidence of hepatotoxicity
  - Without more Category C events
  - Without evidence of other important specific adverse events but:
    - Slight increase in influenza-like events / URTI
    - Slight increase in mild HSV
- Maraviroc is not associated with an adverse outcome in non-CCR5 tropic patients
  - Tropism change in the presence of maraviroc is not associated with adverse effects

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Dose Recommendations

- Based on data from the clinical trials and supported by the exposure response, drug interaction program and population PK analysis from phase 2b/3, the BID dose of maraviroc is recommended to maximize efficacy, particularly in patients with low CD4 counts, high viral loads and few active antiretroviral agents.

Maraviroc Dose	OBT
150 mg BID	PIs (excluding TPV/r) Delavirdine
300 mg BID	TPV/r, NRTIs, enfuvirtide, nevirapine
600 mg BID	Efavirenz (in absence of PIs)

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Treatment-Experienced Patients Infected with CCR5 - Tropic HIV-1

FDA Advisory Committee
Silver Spring, MD
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