



Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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Maraviroc (MVC, Selzentry) (Last updated April 16, 2019; last reviewed April 16, 2019)

For additional information, see Drugs@FDA: <http://www.accessdata.fda.gov/scripts/cder/daf>

Formulations

Tablets: 25 mg, 75 mg, 150 mg, and 300 mg

Oral Solution: 20 mg/mL

Dosing Recommendations

Neonate and Infant Dose:

- Maraviroc is not approved by the Food and Drug Administration (FDA) for use in neonates or infants.

Pediatric Dose:

- Maraviroc is approved by the FDA for use in treatment-experienced children aged ≥ 2 years and weighing ≥ 10 kg

Recommended Maraviroc Dose for Treatment-Experienced Children Aged ≥ 2 Years and Weighing ≥ 10 kg: Tablets or Oral Solution

Weight Band	Twice-Daily Dosing	Oral Solution 20 mg/mL	Tablets
Recommended doses when maraviroc is given with potent cytochrome P450 (CYP) 3A inhibitors (with or without a potent CYP3A inducer), including all protease inhibitors (PIs) except tipranavir/ritonavir (TPV/r)			
10 kg to <20 kg	50 mg	2.5 mL	Two 25-mg tablets
20 kg to <30 kg	75 mg to 80 mg	4 mL	One 75-mg tablet
30 kg to <40 kg	100 mg	5 mL	One 25-mg tablet and one 75-mg tablet
≥ 40 kg	150 mg	7.5 mL	One 150-mg tablet
Recommended doses when maraviroc is given with non-interacting drugs, such as nucleoside reverse transcriptase inhibitors (NRTIs), nevirapine, enfuvirtide, TPV/r, raltegravir			
10 kg to <20 kg	Not recommended. Data are insufficient to make dosing recommendations for children weighing <30 kg and receiving non-interacting medications.		
20 kg to <30 kg	Not recommended. Data are insufficient to make dosing recommendations.		
30 kg to <40 kg	300 mg	15 mL	One 300-mg tablet
≥ 40 kg	300 mg	15 mL	One 300-mg tablet
Recommended doses when maraviroc is given with potent CYP3A inducers (without a potent CYP3A inhibitor), including efavirenz and etravirine			
Children in all weight bands	Not recommended. Data are insufficient to make dosing recommendations.		

Selected Adverse Events

- Nausea, vomiting
- Abdominal pain, diarrhea
- Cough
- Upper respiratory tract infections
- Fever
- Rash
- Hepatotoxicity (which may be preceded by severe rash and/or other signs of systemic allergic reaction)
- Postural hypotension (generally seen in patients with severe renal insufficiency)
- Dizziness

Special Instructions

- Maraviroc is recommended for use in patients who only have CCR5-tropic HIV-1. Conduct testing with a HIV tropism assay (see [Drug-Resistance Testing](#) in the [Adult and Adolescent Antiretroviral Guidelines](#)) before using maraviroc to exclude the presence of CXCR4-tropic or mixed/dual-tropic HIV. Do not use maraviroc if CXCR4-tropic or mixed/dual-tropic HIV is present.
- Maraviroc can be given without regard to food.
- Instruct patients on how to recognize symptoms of allergic reactions or hepatitis.
- Use caution when administering maraviroc to patients with underlying cardiac disease.

Metabolism/Elimination

- Maraviroc is a substrate of CYP3A4. **If a patient is receiving antiretroviral agents or other medications that act as CYP3A inducers or inhibitors, the dose of maraviroc should be adjusted accordingly.**

Recommended Maraviroc Dose for Adults: Tablets

When Coadministered With:	Dose
Potent CYP3A inhibitors (with or without a potent CYP3A inducer), including all PIs except TPV/r	150 mg twice daily
Non-interacting concomitant medications , including NRTIs, enfuvirtide, TPV/r, nevirapine, raltegravir	300 mg twice daily
Potent CYP3A inducers (without a potent CYP3A inhibitor), including efavirenz and etravirine	600 mg twice daily

Maraviroc Dosing in Patients with Hepatic Impairment:

- Use caution when administering maraviroc to patients with hepatic impairment; maraviroc concentrations may be increased in these patients.

Maraviroc Dosing in Patients with Renal Impairment:

- There are no data to recommend specific doses of maraviroc in pediatric patients with mild or moderate renal impairment. Maraviroc is **contraindicated** for pediatric patients with severe renal impairment or end-stage renal disease on regular hemodialysis who are receiving potent CYP3A inhibitors.
- Refer to the manufacturer's prescribing information for the appropriate doses to use in adult patients with renal impairment.

Drug Interactions (see also the [Adult and Adolescent Antiretroviral Guidelines](#) and [HIV Drug Interaction Checker](#))

- *Absorption:* Absorption of maraviroc is slightly reduced with ingestion of a high-fat meal. There were no food restrictions in the adult trials (which used the tablet formulation) or in the pediatric trial (which used both the tablet and oral solution formulations) that demonstrated the efficacy, antiviral activity, and safety of maraviroc. Therefore, maraviroc can be given with or without food.
- *Metabolism:* Maraviroc is a cytochrome P450 (CYP) 3A and p-glycoprotein (P-gp) substrate and requires dose adjustments when administered with medications that modulate CYP3A or P-gp. A patient's medication profile should be carefully reviewed for potential drug interactions before maraviroc is administered; recommended maraviroc doses are based on concomitant medications and their anticipated effect on maraviroc metabolism.

Major Toxicities

- *More common:* Cough, fever, upper respiratory tract infections, rash, musculoskeletal symptoms, abdominal pain, vomiting, diarrhea, and headache. **Dizziness occurred in 12.2% of adults but only 3.2% of children when maraviroc was administered twice daily.**
- *Less common (more severe):* Hepatotoxicity has been reported; some cases were preceded by evidence of a systemic allergic reaction (including pruritic rash, eosinophilia, or elevated levels of immunoglobulin). Serious adverse events (AEs) occurred in <2% of maraviroc-treated adult patients and included cardiovascular abnormalities (e.g., angina, heart failure, myocardial infarction), hepatic cirrhosis or failure, cholestatic jaundice, viral meningitis, pneumonia, myositis, osteonecrosis, and rhabdomyolysis.

Resistance

An HIV tropism assay should be performed before maraviroc is administered to a patient. Clinical failure may also represent the outgrowth of CXCR4-using (naturally resistant) HIV variants.

Pediatric Use

Approval

Maraviroc is approved by the Food and Drug Administration for use in treatment-experienced children aged ≥ 2 years and weighing ≥ 10 kg who have CCR5-tropic HIV-1.¹

Pharmacokinetics and Efficacy

The pharmacokinetics, safety, and efficacy of maraviroc were examined in an international dose-finding and efficacy study (A4001031) that involved treatment-experienced children aged 2 years to < 18 years and weighing ≥ 10 kg who had plasma HIV RNA $> 1,000$ copies/mL. Fifty-one percent of the 103 children who participated in the study had HIV-1 subtype C, 25% had subtype B, and 23% had other subtypes.

In this trial, the maraviroc dose was based on body surface area and the composition of the patient's optimized background therapy. Most participants (90 of 103 participants, or 87%) received maraviroc in combination with potent CYP3A inhibitors, while 10 participants received maraviroc with noninteracting medications and only three participants received maraviroc with CYP3A inducers (without CYP3A inhibitors). The key pharmacologic target (geometric mean C_{average} of > 100 ng/mL) was achieved with both the tablet and oral solution formulations of maraviroc.²

From a mean baseline plasma HIV RNA concentration of $4.4 \log_{10}$ copies/mL, a decrease of $\geq 1.5 \log_{10}$ occurred in all four age-based cohorts. Only two participants discontinued the study due to AEs. The most common maraviroc-related AEs through 48 weeks were diarrhea (which occurred in 20.3% of participants), vomiting (19.8%), and upper respiratory infections (16.2%). At Week 48, 48% of participants had HIV RNA < 48 copies/mL.² The absolute CD4 T lymphocyte cell count and percentage increased in all four subgroups of the study, with an overall median increase of 192 cells/mm³ (interquartile range: 92–352) and 4% (interquartile range: 1–8), respectively.

References

1. Maraviroc [package insert]. Food and Drug Administration. 2016. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208984_022128s017lbl.pdf.
2. Giaquinto C, Mawela MP, Chokeyphaibulkit K, et al. Pharmacokinetics, safety and efficacy of maraviroc in treatment-experienced pediatric patients infected with CCR5-tropic HIV-1. *Pediatr Infect Dis J*. 2018;37(5):459-465. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/29023357>.