

Maraviroc (MVC, Selzentry)

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Formulations																															
<p>Oral Solution: 20 mg/mL</p> <p>Tablets: 25 mg, 75 mg, 150 mg, 300 mg</p> <p>For additional information, see Drugs@FDA or DailyMed.</p>																															
Dosing Recommendations		Selected Adverse Events																													
<ul style="list-style-type: none"> Maraviroc (MVC) is approved by the U.S. Food and Drug Administration (FDA) for use, in combination with other antiretroviral agents, for the treatment of CCR5-tropic HIV-1 infection in infants born full term weighing ≥ 2 kg, children, adolescents, and adults. <p>Recommended Maraviroc Dose for Full-Term Infants and Treatment-Experienced Children and Adolescents Weighing ≥ 2 kg: Tablets or Oral Solution</p> <table border="1"> <thead> <tr> <th>Weight Band</th> <th>Twice-Daily Dosing</th> <th>Oral Solution 20 mg/mL</th> <th>Tablets</th> </tr> </thead> <tbody> <tr> <td colspan="4">Recommended doses when MVC is given with non-interacting drugs, such as nucleoside reverse transcriptase inhibitors (NRTIs), nevirapine (NVP), enfuvirtide (T-20), and raltegravir (RAL)</td> </tr> <tr> <td>2 kg to <4 kg</td> <td>30 mg</td> <td>1.5 mL</td> <td>N/A</td> </tr> <tr> <td>4 kg to <6 kg</td> <td>40 mg</td> <td>2 mL</td> <td>N/A</td> </tr> <tr> <td>6 kg to <10 kg</td> <td>100 mg</td> <td>5 mL</td> <td>One 25-mg tablet and one 75-mg tablet</td> </tr> <tr> <td>10 kg to 14 kg</td> <td>150 mg</td> <td>7.5 mL</td> <td>One 150-mg tablet</td> </tr> <tr> <td>14 kg to <30 kg</td> <td>200 mg</td> <td>10 mL</td> <td>One 150-mg tablet and two 25-mg tablets</td> </tr> </tbody> </table>		Weight Band	Twice-Daily Dosing	Oral Solution 20 mg/mL	Tablets	Recommended doses when MVC is given with non-interacting drugs, such as nucleoside reverse transcriptase inhibitors (NRTIs), nevirapine (NVP), enfuvirtide (T-20), and raltegravir (RAL)				2 kg to <4 kg	30 mg	1.5 mL	N/A	4 kg to <6 kg	40 mg	2 mL	N/A	6 kg to <10 kg	100 mg	5 mL	One 25-mg tablet and one 75-mg tablet	10 kg to 14 kg	150 mg	7.5 mL	One 150-mg tablet	14 kg to <30 kg	200 mg	10 mL	One 150-mg tablet and two 25-mg tablets	<ul style="list-style-type: none"> 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 	
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Special Instructions																															
<ul style="list-style-type: none"> MVC is recommended for use in patients who have only CCR5-tropic HIV-1. Before using MVC, conduct testing with an HIV tropism assay (see Drug-Resistance Testing in the Adult and Adolescent Antiretroviral Guidelines) to exclude the presence of CXCR4-tropic or mixed/dual-tropic HIV. Do not use MVC if CXCR4-tropic or mixed/dual-tropic HIV is present. MVC can be given without regard to food. Instruct patients on how to recognize symptoms of allergic reactions or hepatitis. Use caution when administering MVC to patients with underlying cardiac disease. 																															

30 kg to <40 kg	300 mg	15 mL	One 300-mg tablet	<p style="text-align: center;">Metabolism/Elimination</p> <ul style="list-style-type: none"> MVC 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 MVC should be adjusted accordingly. <p>Maraviroc Dosing in Patients with Hepatic Impairment</p> <ul style="list-style-type: none"> Use caution when administering MVC to patients with hepatic impairment; MVC concentrations may be increased in these patients. <p>Maraviroc Dosing in Patients with Renal Impairment</p> <ul style="list-style-type: none"> No data recommend specific doses of MVC for pediatric patients with mild or moderate renal impairment. MVC is contraindicated for pediatric patients with severe renal impairment or end-stage renal disease who are on regular hemodialysis and who are receiving potent CYP3A inhibitors. Refer to the manufacturer's prescribing information for the appropriate doses to use in adolescent and adult patients with renal impairment.
≥40 kg	300 mg	15 mL	One 300-mg tablet	
Recommended doses when MVC is given with potent cytochrome P450 (CYP) 3A inhibitors (with or without a potent CYP3A inducer), including all protease inhibitors (PIs)				
2 kg to <10 kg	Not recommended. Data are insufficient to make dosing recommendations for infants weighing <10 kg and receiving a potent P450 CYP3A inhibitor.			
10 kg to <20 kg	50 mg	2.5 mL	Two 25-mg tablets	
20 kg to <30 kg	75–80 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 MVC is given with potent CYP3A inducers (without a potent CYP3A inhibitor), including efavirenz (EFV) and etravirine (ETR)				
Infants and children and adolescents in all weight bands	Not recommended. Data are insufficient to make dosing recommendations.			
Recommended Maraviroc Dose for Adults: Tablets				
When Coadministered With		Dose		
Non-interacting concomitant medications, including NRTIs, T-20, NVP, and RAL		300 mg twice daily		

Potent CYP3A inhibitors (with or without a potent CYP3A inducer), including all PIs	150 mg twice daily	
Potent CYP3A inducers (without a potent CYP3A inhibitor), including EFV and ETR	600 mg twice daily	

Drug Interactions

Additional information about drug interactions is available in the [Adult and Adolescent Antiretroviral Guidelines](#) and the [HIV Drug Interaction Checker](#).

- *Absorption:* Absorption of maraviroc (MVC) is slightly reduced with ingestion of a high-fat meal. Food restrictions were not part of either the adult trials (which used the tablet formulation) or the pediatric trial (which used both the tablet and oral solution formulations) that demonstrated the efficacy, antiviral activity, and safety of MVC. Therefore, MVC can be given with or without food.
- *Metabolism:* MVC 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 MVC is administered; recommended MVC doses are based on concomitant medications and their anticipated effect on MVC 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 MVC 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 MVC-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.

Mechanism of Action

MVC is a CCR5 receptor antagonist that selectively binds to the human chemokine receptor CCR5 on the cell membrane, preventing interaction between HIV-1 gp120 and CCR5 tropic HIV-1, inhibiting viral entry into the cell.

Resistance

An HIV tropism assay should be performed before MVC is administered to a patient. Clinical failure may also represent the outgrowth of CXCR4-using (naturally resistant) HIV variants. However, in circumstances when MVC is needed for presumptive HIV therapy for full-term neonates at high risk

of perinatal HIV transmission, initiation of MVC should not be deferred until assay results are available, and consultation with an HIV expert is recommended.

Pediatric Use

Approval

MVC was recently approved by the U.S. Food and Drug Administration (FDA) for treatment in full-term infants weighing ≥ 2 kg when used in conjunction with other antiretroviral drugs.¹ MVC had previously been approved by the FDA for use in children ≥ 2 years and weighing ≥ 10 kg, as well as adolescents and adults who have CCR5-tropic HIV-1.²

Pharmacokinetics and Efficacy

The International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT 2007) study evaluated the pharmacokinetics (PK) and safety of MVC added to a 6-week prophylactic antiretroviral regimen to prevent perinatal HIV transmission of HIV among infants born to mothers living with HIV.² Analyses were stratified by exposure to efavirenz (EFV), either *in utero* or through breastmilk versus non-EFV exposure. The MVC exposure target was average plasma concentration (C_{avg}) ≥ 75 ng/mL, as determined by adult treatment studies. MVC oral solution was dosed at 8 mg/kg twice daily for the first 6 weeks of life. Among 25 infants with evaluable PK data, 12 of whom were EFV-exposed, 67% of the EFV-exposed infants achieved a $C_{avg} \geq 75$ ng/mL at Week 1, whereas 77% of the EFV-unexposed infants had a $C_{avg} \geq 75$ ng/mL. At Week 4, the proportion of infants achieving a $C_{avg} \geq 75$ ng/mL declined to 42% among EFV-exposed infants and 31% among EFV-unexposed infants. No infants in the study met safety endpoints or discontinued MVC during the study and no infants acquired HIV. The FDA recommendation for MVC dosing among children >6 weeks of life but younger than 2 years of age is based on modeling using PK data from the IMPAACT 2007 study. When considering the use of MVC for neonates and infants, a pediatric HIV specialist should be consulted.

PK, safety, and efficacy of MVC for treatment-experienced children, ages 2 years to <18 years and weighing ≥ 10 kg, who had plasma HIV RNA $>1,000$ copies/mL, were examined in an international dose-finding and efficacy study (A4001031). Of the 103 children who participated in the study, 51% had HIV-1 subtype C, 25% had subtype B, and 23% had other subtypes.

In this trial, the MVC dose was based on body surface area and the composition of the patient's optimized background therapy. Most participants, [90 of 103 participants (87%)], received MVC in combination with potent CYP3A inhibitors; 10 participants received MVC with noninteracting medications; and only 3 participants received MVC with CYP3A inducers (without CYP3A inhibitors). The key pharmacologic target (geometric mean C_{avg} of >100 ng/mL) was achieved with both the tablet and oral solution formulation of MVC.³

From a mean baseline plasma HIV RNA concentration of 4.4 \log_{10} copies/mL, a decrease of ≥ 1.5 \log_{10} occurred in all four age-based cohorts. Only two participants discontinued the study due to AEs. The most common MVC-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.³ The absolute CD4 T lymphocyte cell count and percentage increased in all four subgroups of the study, with overall median increases of 192 cells/mm³ (interquartile range [IQR] 92–352 cells/mm³) and 4% (IQR 1% to 8%), respectively.

References

1. Maraviroc (Selzentry) [package insert]. Food and Drug Administration. 2020. Available at:
https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/022128Orig1s019,208984Orig1s002lbl.pdf.
2. Rosebush JC, Best BM, Chadwick EG, et al. Pharmacokinetics and safety of maraviroc in neonates. *AIDS*. 2021;35(3):419-427. Available at:
<https://www.ncbi.nlm.nih.gov/pubmed/33252481>.
3. Giaquinto C, Mawela MP, Chokephaibulkit 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>.