Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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**Maraviroc (MVC, Selzentry)** *(Last updated May 22, 2018; last reviewed May 22, 2018)*

For additional information see Drugs@FDA: [http://www.accessdata.fda.gov/scripts/cder/daf](http://www.accessdata.fda.gov/scripts/cder/daf)

**Formulations**

**Tablets:** 25 mg, 75 mg, 150 mg, and 300 mg  
**Oral Solution:** 20 mg/mL

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**Dosing Recommendations**

**Neonate and Infant Dose:**  
- Not approved for use in neonates or infants

**Pediatric Dose:**  
- Approved 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**

<table>
<thead>
<tr>
<th>Weight Band</th>
<th>Twice-Daily Dosing</th>
<th>Liquid 20 mg/mL</th>
<th>Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 kg to &lt;20 kg</td>
<td>50 mg</td>
<td>2.5 mL</td>
<td>Two 25-mg tablets</td>
</tr>
<tr>
<td>20 kg to &lt;30 kg</td>
<td>75 mg</td>
<td>4 mL</td>
<td>One 75-mg tablet</td>
</tr>
<tr>
<td>30 kg to &lt;40 kg</td>
<td>100 mg</td>
<td>5 mL</td>
<td>One 25-mg tablet and one 75-mg tablet</td>
</tr>
<tr>
<td>&gt;40 kg</td>
<td>150 mg</td>
<td>7.5 mL</td>
<td>One 150-mg tablet</td>
</tr>
</tbody>
</table>

When given with potent cytochrome P (CYP) 3A inhibitors (with or without a potent CYP3A inducer), including elvitegravir/ritonavir (EVG/r) and 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 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

When given with nucleoside reverse transcriptase inhibitors (NRTIs), enfuvirtide, TPV/r, nevirapine, raltegravir, and other drugs that are not potent CYP3A inhibitors or inducers:

- 10 kg to <20 kg: Not recommended
- 20 kg to <30 kg: Not recommended
- 30 kg to <40 kg: 300 mg 15 mL One 300-mg tablet
- >40 kg: 300 mg 15 mL One 300-mg tablet

When given with potent CYP3A inducers including efavirenz and etravirine (without a potent CYP3A inhibitor):

- Children in all weight bands: Not recommended

**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 patients with only CCR5-tropic HIV-1. Conduct testing with HIV tropism assay (see Drug-Resistance Testing in the Adult and Adolescent 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**

- Cytochrome P450 3A4 (CYP3A4) substrate

**Maraviroc Dosing in Patients with Hepatic Impairment:**

- Use caution when administering maraviroc to patients with hepatic impairment; maraviroc concentrations may be increased.
**Drug Interactions** (see also the Adult and Adolescent 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) and in the pediatric trial (which used both 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 P (CYP) 3A and p-glycoprotein (P-gp) substrate and requires dose adjustments when administered with CYP- or P-gp–modulating medications. A patient’s medication profile should be carefully reviewed for potential drug interactions before administration of maraviroc; 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 is seldom reported in children.

- **Less common (more severe):** Hepatotoxicity that may be preceded by evidence of a systemic allergic reaction (such as pruritic rash, eosinophilia, or elevated immunoglobulin) has been reported. 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**

HIV tropism assay should be performed before use. Clinical failure may also represent the outgrowth of CXCR4-using (naturally resistant) HIV variants. The International Antiviral Society-USA (IAS-USA) maintains a list of updated resistance mutations.

**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

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1. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

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weighing \( \geq 10 \) kg) who had HIV-1 plasma 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 optimized background therapy. Most participants (90/103 participants, or 87%) received maraviroc in combination with potent CYP3A inhibitors, 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 \( C_{\text{average}} \) of >100 ng/mL) was achieved with both the tablet and oral solution formulations of maraviroc.

From a mean baseline plasma HIV-1 RNA 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 (16.5%), vomiting (16.5%), and upper respiratory infections (13.6%). At Week 48, 48% of participants had HIV-1 RNA <48 copies/mL. Of the participants on long-term follow-up at Week 144, 86% had HIV-1 RNA levels of <48 copies/mL.

References