**Saquinavir (SQV, Invirase)** *(Last updated April 27, 2017; last reviewed April 27, 2017)*

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

### Formulations
- **Capsules:** 200 mg
- **Tablets:** 500 mg

### Dosing Recommendations

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

**Pediatric Dose:**
- Not approved for use in children and adolescents aged <16 years.

**Investigational Doses in Treatment-Experienced Children:**
- Saquinavir must be boosted with ritonavir.

**Aged <2 Years:**
- No dose has been determined.

**Aged ≥2 Years (Conditional Dosing Based on Limited Data; See Text):**

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Dose Saquinavir plus Ritonavir</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 to &lt;15 kg</td>
<td>Saquinavir 50 mg/kg plus ritonavir 3 mg/kg, both twice daily</td>
</tr>
<tr>
<td>15 to &lt;40 kg</td>
<td>Saquinavir 50 mg/kg plus ritonavir 2.5 mg/kg, both twice daily</td>
</tr>
<tr>
<td>≥40 kg</td>
<td>Saquinavir 50 mg/kg plus ritonavir 100 mg, both twice daily</td>
</tr>
</tbody>
</table>

**Adolescent (Aged ≥16 years) and Adult Dose:**
- Saquinavir should **only** be used in combination with ritonavir.
- Saquinavir 1000 mg plus ritonavir 100 mg, both twice daily.

### Selected Adverse Events
- Gastrointestinal intolerance, nausea, and diarrhea
- Headache
- Elevated transaminases
- Hyperlipidemia
- Hyperglycemia
- Fat maldistribution
- Increased bleeding episodes in patients with hemophilia
- PR interval prolongation, QT interval prolongation, and ventricular tachycardia (**Torsades de Pointes**) have been reported.

### Special Instructions
- Administer within 2 hours after a full meal.
- Sun exposure can cause photosensitivity reactions; advise patients to use sunscreen or protective clothing.
- Pre-therapy electrocardiogram is recommended and saquinavir is contraindicated in patients with a prolonged QT interval.

### Metabolism/Elimination
- Cytochrome P (CYP) 450 3A4 and inhibitor, 90% metabolized in the liver.
- Use in patients with hepatic impairment: use with caution.

### Drug Interactions
(see also the [Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents](http://www.hiv-druginteractions.org/) and [http://www.hiv-druginteractions.org/](http://www.hiv-druginteractions.org/))

- Saquinavir is both a substrate and inhibitor of the CYP3A4 system. Potential exists for multiple drug interactions. Co-administration of saquinavir is contraindicated with drugs that are highly dependent on CYP3A clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events.
- Before administration, a patient’s medication profile should be carefully reviewed for potential drug interactions.
Antiretroviral Therapy and Medical Management of Children Living with HIV does not recommend the use were considered for salvage therapy in children prior to the emergence of the new classes of antiretroviral
Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection and PR intervals. Rare cases of
In most average C_{\text{min}} upon toxicity. Most C_{\text{min}} values for saquinavir were above the desired trough value of 0.1 mg/L. The
adequate load to <50 copies/mL. Drug monitoring established used was an dosed extensively as initiated on saquinavir/lopinavir/ritonavir
children, therapy concentration twice dose administered whereas daily with ritonavir boosting, demonstrated that drug exposure was lower in children younger than 2 years PK
Studies Pharmacokinetics in inhibi tors Efficacy
Saquinavir has been studied with nucleoside reverse transcriptase inhibitors (NRTIs) and other protease inhibitors (PIs) in HIV-infected children.\textsuperscript{1,6} Saquinavir/ritonavir and saquinavir/lopinavir/ritonavir regimens were considered for salvage therapy in children prior to the emergence of the new classes of antiretroviral medications. As dual PI therapy is no longer recommended in adult or pediatric guidelines, The Panel on
Antiretroviral Therapy and Medical Management of Children Living with HIV does not recommend the use of saquinavir/lopinavir/ritonavir combination.\textsuperscript{1,3,9}

Pharmacokinetics
Studies suggest that saquinavir should not be used without ritonavir boosting. A pharmacokinetic (PK) analysis of 5 children younger than 2 years and 13 children aged 2 to 5 years, using a dose of 50 mg/kg twice daily with ritonavir boosting, demonstrated that drug exposure was lower in children younger than 2 years whereas drug exposure was adequate in those aged 2 to 5 years.\textsuperscript{10} For this reason, saquinavir should not be administered to children aged <2 years. In children aged ≥2 years, a dose of 50 mg/kg twice daily (maximum dose = 1000 mg) boosted with ritonavir 3 mg/kg twice daily (patients weighing 5 to <15 kg) or 2.5 mg/kg twice daily (patients weighing 15–40 kg) resulted in area under the curve and steady-state trough plasma concentration (C_{\text{trough}}) values similar to those in older children\textsuperscript{7,8} and adults.

In a study of 50 Thai children, saquinavir/lopinavir/ritonavir was initiated as second-line therapy based on extensive NRTI resistance (saquinavir was dosed at 50 mg/m\textsuperscript{2} body surface area and lopinavir/ritonavir was dosed at 230/57.5 mg/m\textsuperscript{2} body surface area, all twice daily). After 96 weeks, 74\% of the children achieved an undetectable plasma RNA load at <50 copies/mL. Therapeutic drug monitoring was used to establish adequate minimum plasma concentration (C_{\text{min}}) values and to aid with alterations in drug dosage based upon toxicity. Most C_{\text{min}} values for saquinavir were above the desired trough value of 0.1 mg/L. The average C_{\text{min}} throughout 96 weeks for saquinavir was 1.37 mg/L, and when saquinavir doses were adjusted, most were decreased by an average of 21\% (8 mg/kg).\textsuperscript{7,8}

Toxicity
In a healthy adult volunteer study, saquinavir/ritonavir use was associated with increases in both QT and PR intervals.\textsuperscript{11,12} Rare cases of Torsades de Pointes and complete heart block have been reported
in post-marketing surveillance. Saquinavir/ritonavir is not recommended for patients with any of the following conditions: documented congenital or acquired QT prolongation, pretreatment QT interval of >450 milliseconds, refractory hypokalemia or hypomagnesemia, complete atrioventricular block without implanted pacemakers, at risk of complete AV block, or receiving other drugs that prolong QT interval. An electrocardiogram is recommended before initiation of therapy with saquinavir and should be considered during therapy.

References