Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection

Downloaded from https://aidsinfo.nih.gov/guidelines on 8/27/2017

Visit the AIDSinfo website to access the most up-to-date guideline.

Register for e-mail notification of guideline updates at https://aidsinfo.nih.gov/e-news.
Ritonavir (RTV, Norvir) *(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

**Oral Solution (Contains 43% Alcohol by Volume):** 80 mg/mL  
**Tablets:** 100 mg

### Dosing Recommendations

**Ritonavir as a Pharmacokinetic (PK) Enhancer:**a  
- Ritonavir is used as a PK enhancer of other protease inhibitors (PIs). The recommended dose of ritonavir varies and is specific to the drug combination selected. See dosing information for specific PIs.

*a Ritonavir has antiviral activity but is not used as an antiviral agent (see text).*

### Selected Adverse Events

- Gastrointestinal intolerance, nausea, vomiting, diarrhea  
- Paresthesia (circumoral and extremities)  
- Hyperlipidemia, especially hypertriglyceridemia  
- Hepatitis  
- Asthenia  
- Taste perversion  
- Hyperglycemia  
- Fat maldistribution  
- Possible increased bleeding episodes in patients with hemophilia  
- Toxic epidermal necrolysis and Stevens-Johnson syndrome

### Special Instructions

- Administer ritonavir with food to increase absorption and reduce gastrointestinal adverse effects.  
- Do not administer ritonavir with cobicistat or drugs that contain cobicistat (e.g., Stribild, Genvoya, Prezobix, Evotaz).  
- If ritonavir is prescribed with didanosine, administer the drugs 2 hours apart.  
- Do not refrigerate ritonavir oral solution; store at 68°F to 77°F (20°C to 25°C). Shake the solution well before use.  
- To Increase Tolerability of Ritonavir Oral Solution in Children:  
  - Mix solution with milk, chocolate milk, or vanilla or chocolate pudding or ice cream.  
  - Before administration, give a child ice chips, a Popsicle, or spoonfuls of partially frozen orange or grape juice concentrate to dull the taste buds, or give peanut butter to coat the mouth.
Drug Interactions (see also the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents and http://iasusa.org/sites/default/files/tam/october_november_2015.pdf#page=10)

- **Metabolism:** Ritonavir is extensively metabolized by and is one of the most potent inhibitors of hepatic cytochrome P450 3A (CYP3A). There is potential for multiple drug interactions with ritonavir.
- Before ritonavir is administered, a patient’s medication profile should be carefully reviewed for potential interactions with ritonavir and overlapping toxicities with other drugs.
- Ritonavir and cobicistat are not interchangeable and may result in different drug interactions.2
- Avoid concomitant use of intranasal or inhaled fluticasone because of reports of adrenal insufficiency.2 Use caution when prescribing ritonavir with other inhaled steroids; limited data suggest that beclomethasone may be a suitable alternative to fluticasone when an inhaled/intranasal corticosteroid is required for a patient who is taking ritonavir.3,4

**Major Toxicities**

- **More common:** Nausea, vomiting, diarrhea, headache, abdominal pain, anorexia, circumoral paresthesia, lipid abnormalities
- **Less common (more severe):** Exacerbation of chronic liver disease, fat maldistribution
- **Rare:** New-onset diabetes mellitus, hyperglycemia, ketoacidosis, exacerbation of preexisting diabetes mellitus, spontaneous bleeding in hemophiliacs, pancreatitis, and hepatitis (life-threatening in rare cases). Allergic reactions, including bronchospasm, urticaria, and angioedema. Toxic epidermal necrolysis and Stevens-Johnson syndrome have occurred.5

**Resistance**

Resistance to ritonavir is not clinically relevant when the drug is used as a pharmacokinetic (PK) enhancer of other antiretroviral (ARV) medications.
Pediatric Use

Approval

Ritonavir has been approved by the Food and Drug Administration for use in the pediatric population.

Efficacy: Effectiveness in Practice

Use of ritonavir as the sole protease inhibitor (PI) in antiretroviral therapy in children is not recommended. Although ritonavir has been well studied in children as an ARV agent, it is no longer used as a sole PI for therapy because ritonavir is associated with a higher incidence of gastrointestinal toxicity and has a greater potential for drug-drug interactions than other PIs. In addition, poor palatability of the liquid preparation and large pill burden with the tablets (adult dose is 6 tablets twice daily) limit its use as a sole PI. However, in both children and adults, ritonavir is recommended as a PK enhancer for use with other PIs. Ritonavir is a CYP3A4 inhibitor and functions as a PK enhancer by slowing the metabolism of the PIs.

Dosing

Pediatric dosing regimens including boosted fosamprenavir, tipranavir, darunavir, atazanavir and a PI co-formulation, lopinavir/ritonavir (LPV/r), are available (see individual PIs for more specific information).

Toxicity

Full-dose ritonavir has been shown to prolong the PR interval in a study of healthy adults who were given ritonavir at 400 mg twice daily.4 Potentially life-threatening arrhythmias in premature newborn infants treated with LPV/r have been reported; the use of LPV/r is not recommended until the gestational age of 42 weeks.6,7 Co-administration of ritonavir with other drugs that prolong the PR interval (e.g., macrolides, quinolones, methadone) should be undertaken with caution because it is unknown how co-administering any of these drugs with ritonavir will affect the PR interval. In addition, ritonavir should be used with caution in patients who may be at increased risk of developing cardiac conduction abnormalities, such as those with underlying structural heart disease, conduction system abnormalities, ischemic heart disease, or cardiomyopathy.

References


