



## The Annotated Bibliography of the UCSF HIV Solid Organ Transplantation Project

### ARV Dosing in End Stage Renal Disease

1. Jayasekara, D., Aweeka, F. T., Rodriguez, R., Kalayjian, R. C., Humphreys, M. H., & Gambertoglio, J. G. (1999). Antiviral therapy for HIV patients with renal insufficiency. *Journal of Acquired Immune Deficiency Syndromes*, 21(5), 384-95.

ABSTRACT: Patients with HIV infection and HIV-related opportunistic infections are treated extensively with a spectrum of drugs. Introduction of new antiretroviral drugs, such as protease inhibitors and nonnucleoside reverse transcriptase inhibitors in addition to nucleoside reverse transcriptase inhibitors, has created exciting dimensions in treatment strategies. Renal dysfunction is also common in HIV-infected patients. Because some drugs used in HIV are primarily excreted unchanged by the kidney, dose adjustments are necessary in patients with renal insufficiency. Drugs such as foscarnet, cidofovir and adefovir are directly nephrotoxic, whereas acyclovir can crystallize in the kidneys, and indinavir may cause nephrolithiasis. This paper reviews the impact of renal insufficiency on pharmacokinetics of antiviral drugs used in HIV disease and discusses dosage recommendations needed to avoid toxicity. Finally, we summarize the effects of dialysis on removal of these drugs.

2. Renal Dosing of Antiretrovirals (table). (1999). Rodriguez, R. A., and Schoenfeld, P. A., Renal Manifestations of HIV Infection. In Cohen, P. T., Sande, M. A., and Volberding, P. A. (Eds.), *The AIDS Knowledge Base: A Textbook on HIV Disease from the University of California, San Francisco and the San Francisco General Hospital* (3<sup>rd</sup> ed.), New York: Lippincott, Williams & Wilkins.

The AIDS Knowledge Base can be found on the web at: <http://hivinsite.ucsf.edu//akb/>

The URL for this table is <http://hivinsite.ucsf.edu/akb/current/05renal/toctable1.html>

3. GlaxoWellcome. (2000). *Administration and Safety of Efavirenz in Patients with Renal Impairment*. Research Triangle Park, NC: GlaxoWellcome.
4. GlaxoWellcome. (2000). *Administration of Zidovudine in Patients with Renal Impairment*. Research Triangle Park, NC: GlaxoWellcome.
5. GlaxoWellcome. (2000). *Pharmacokinetics of Adefovir in Adults and Pediatrics*. Research Triangle Park, NC: GlaxoWellcome.
6. GlaxoWellcome. (2000). *Use of Zidovudine (Zidovudine) in Patients with End-Stage Renal Disease (ESRD) on Dialysis*. Research Triangle Park, NC: GlaxoWellcome.

7. **GlaxoWellcome. (2000). *Potential Safety Concerns with the large amount of propylene glycol in AGENERASE (amprenavir) Oral Solution*. Research Triangle Park, NC: GlaxoWellcome Inc.**
8. **Merck. (2000). *CRIXIVAN (Indinavir sulfate) Dosing*. West Point, PA: Merck & Co., Inc.**

**Anti-Retroviral Adult Dosage Guideline**

Anti-Retroviral Agents	Adult Dosages	Renal Function Adjustment	Storage Instructions	Food Considerations																								
<b>Abacavir (Ziagen <math>\bar{O}</math>)</b> <b>Yellow, capsule-shaped tablet:</b> 300mg  <b>Oral Solution:</b> 20mg/mL	300mg BID (2 tab/day)  <b>Hypersensitivity Registry:</b> <b>1-800-270-0425</b>	Not Necessary	<b>Tablets:</b> Room temperature  <b>Oral Solution:</b> Room temperature or refrigerate, DO NOT FREEZE	Can be taken with or without food																								
<b>Didanosine (ddI, Videx<sup>a</sup>)</b>  <b>White, round tablets:</b> 25, 50, 100, 150 mg; 200 mg tablets (for once daily dosing only) <b>Sachets:</b> 167 & 250 mg;  <b>Pediatric Suspension:</b> 2 & 4 Gm Powder, final solution: 10mg/mL	> 60 kg 200 mg BID (4 tab/day)*, or 400 mg qD (2 tab/day), or Sachet: 250mg bid  < 60 kg 125 mg BID (4 tab/day)*, or 250mg qD (1-100mg tab + 1-150mg tab or 1-200mg tab + 1-50mg tab), or Sachet: 167 mg bid  *bid is the preferred dosing schedule	≥ 60 kg <table border="0"> <tr> <td>CrCl (ml/min)</td> <td>Tablet</td> <td>Sachet</td> </tr> <tr> <td>30-59</td> <td>100mg BID or 200mg QD</td> <td>100mg BID</td> </tr> <tr> <td>10-29</td> <td>150 mg QD</td> <td>167 mg QD</td> </tr> <tr> <td>&lt; 10</td> <td>100 mg QD</td> <td>100mg QD</td> </tr> </table> < 60 kg <table border="0"> <tr> <td>CrCl (ml/min)</td> <td>Tablet</td> <td>Sachet</td> </tr> <tr> <td>30-59</td> <td>150mg QD or 75 mg BID</td> <td>100mg BID</td> </tr> <tr> <td>10-29</td> <td>100 mg QD</td> <td>100 mg QD</td> </tr> <tr> <td>&lt; 10</td> <td>75 mg QD</td> <td>100mg QD</td> </tr> </table> <b>CAPD or Hemodialysis Pt:</b> 1/4 daily dose per day	CrCl (ml/min)	Tablet	Sachet	30-59	100mg BID or 200mg QD	100mg BID	10-29	150 mg QD	167 mg QD	< 10	100 mg QD	100mg QD	CrCl (ml/min)	Tablet	Sachet	30-59	150mg QD or 75 mg BID	100mg BID	10-29	100 mg QD	100 mg QD	< 10	75 mg QD	100mg QD	Room temp. in tightly closed container  <b>Tablet:</b> stable for 1hr in room temp after dispersed in apple juice or water  <b>Sachet:</b> stable for 4hr after dissolved in water  <b>Suspension:</b> Mix with antacid, store in refrigerator for up to 30 days	Empty stomach; ≥ 1/2 hr before or ≥ 2 hr after meals; space apart with all protease inhibitors  Take w/ water or apple juice
CrCl (ml/min)	Tablet	Sachet																										
30-59	100mg BID or 200mg QD	100mg BID																										
10-29	150 mg QD	167 mg QD																										
< 10	100 mg QD	100mg QD																										
CrCl (ml/min)	Tablet	Sachet																										
30-59	150mg QD or 75 mg BID	100mg BID																										
10-29	100 mg QD	100 mg QD																										
< 10	75 mg QD	100mg QD																										
<b>Lamivudine (3TC, Epivir<math>\bar{O}</math>)</b> <b>White, diamond shape tablet:</b> 150 mg <b>Oral solution:</b> 10 mg/ml  Also see: Combivir <sup>TM</sup> below	150 mg BID (2 tab/day)	<table border="0"> <tr> <td>CrCl (ml/min)</td> <td>Dose</td> </tr> <tr> <td>30-49</td> <td>150mg qd</td> </tr> <tr> <td>15-29</td> <td>150mg qd, then 100 qd</td> </tr> <tr> <td>5-14</td> <td>150 mg qd, then 50 qd</td> </tr> <tr> <td>&lt; 5</td> <td>50 qd, then 25 qd</td> </tr> </table> No data on hemodialysis	CrCl (ml/min)	Dose	30-49	150mg qd	15-29	150mg qd, then 100 qd	5-14	150 mg qd, then 50 qd	< 5	50 qd, then 25 qd	Room temperature	No specific consideration														
CrCl (ml/min)	Dose																											
30-49	150mg qd																											
15-29	150mg qd, then 100 qd																											
5-14	150 mg qd, then 50 qd																											
< 5	50 qd, then 25 qd																											
<b>Stavudine (d4T, Zerit<math>\bar{O}</math>)</b>  40mg-dark orange cap; 30mg-light & dark orange cap; 20mg-light brown cap; 15mg-light yellow & dark red cap  <b>Oral soln:</b> 1 mg/ml	> 60 kg 40 mg BID (2 tab/day)  < 60 kg 30 mg BID (2 tab/day)	<table border="0"> <tr> <td>CrCl</td> <td>Dose</td> </tr> <tr> <td>26-50</td> <td>20 mg q12h</td> </tr> <tr> <td>≤ 25</td> <td>20 mg q24h</td> </tr> </table> No data on hemodialysis	CrCl	Dose	26-50	20 mg q12h	≤ 25	20 mg q24h	Room temperature  <b>Oral suspension:</b> Store in refrigerator after reconstitution. Stable for up to 30 days	No specific considerations																		
CrCl	Dose																											
26-50	20 mg q12h																											
≤ 25	20 mg q24h																											
<b>Zalcitabine (ddC, Hivid<sup>b</sup>)</b> 0.75mg – white, oblong tab 0.375mg - beige, oblong tab	> 60 kg 0.75 mg TID (3 tab/day)  < 60 kg 0.375 mg TID (3 tab/day)	<table border="0"> <tr> <td>CrCl</td> <td>Dose</td> </tr> <tr> <td>10-40</td> <td>0.75 mg BID</td> </tr> <tr> <td>&lt; 10</td> <td>0.75 mg qD</td> </tr> </table>	CrCl	Dose	10-40	0.75 mg BID	< 10	0.75 mg qD	Room temperature	No specific consideration																		
CrCl	Dose																											
10-40	0.75 mg BID																											
< 10	0.75 mg qD																											

		No data on hemodialysis		
<b>Zidovudine (ZDV, AZT, Retrovir<sup>®</sup>)</b> Blue & white cap – 100 mg; White, round tab – 300 mg;  <b>Oral Syrup:</b> 50mg/5ml  <b>IV</b> - 10 mg/ml See Combivir™ below	200 mg TID (6 cap/day), or 300 mg BID (2 tab/day); or  [100 mg 5x/day]	100 mg TID in pts with severe renal impairment  Hemodialysis: 100 mg TID	Room temperature	Not to be taken with meals if possible - but not absolutely necessary (≥ 30 min before or 2 hr after meals)
<b>ZDV 300 mg + 3TC 150 mg (Combivir<sup>®</sup>)</b> white, oblong tab	One tablet BID (2 tab/day)	<b>Not recommended in pts where dosage adjustment is required, ie pts w/ renal insufficiency, low body weight (&lt; 50kg), or experiencing dose-limiting side effects</b>	Room temperature	With or without food
<b>Delavirdine (Rescriptor<sup>®</sup>)</b> White oblong tab – 100 & 200mg	400 mg TID (12 tab/day)	Not Necessary  Hemodialysis - no effect	Room temperature	W/ or w/o food, avoid taking w/ antacids, dDI, or H2-blockers; acidic beverages ↑ absorption; Can mix 4 tablets in 3 oz of water to make a dispersion (drink promptly)
<b>Efavirenz (Sustiva<sup>®</sup>)</b> Gold cap – 200mg White cap – 100mg Gold & white cap – 50mg	600 mg qHS (3 cap/day)	Not necessary	Room temperature	Avoid high fat meal; no restriction regarding meal schedule & dose administration
<b>Nevirapine (Viramune<sup>®</sup>)</b> White oval tab - 200 mg Oral suspension – 50 mg/5 mL	200 mg qD x 14 days, then 200 mg BID (2 tab/day)	Not Necessary Hemodialysis - data not available	Room temperature	No specific consideration
<b>Amprenavir (Agenerase™)</b>  White capsule – 50mg, 150mg Oral Solution – 15 mg/mL  Oral capsule & solution are not interchangeable on a mg per mg basis	1,200 mg q12h (16 capsules/day)	Not necessary	Room temperature	No food restriction  Each daily dose contains 1744 IU of Vitamin E; Vitamin E supplementatin should be discontinued  Oral solution contains a large amount of propylene glycol – contraindicated in children < 4yo, pregnant women, pts w/ renal or hepatic failure, & pts treated w/ disulfiram or metronidazole
<b>Indinavir (Crixivan<sup>®</sup>)</b>  Off white capsules – 200 mg , 333 mg & 400 mg	800 mg q8h (6 cap/day)	Not Necessary  No data on dialysis	Store in tightly closed original container .  <b>Do not discard dessicant.</b>	Empty stomach or w/ light, low fat meals - at least 1 hr apart from dDI dose  <b>Drink 1-2 liters of fluid per day with or w/o food if taken with</b>

<p><b>Lopinavir (Kaletra<sup>®</sup>)</b>   <b>Orange soft get capsules – 133mg lopinavir + 33 mg ritonavir per capsule</b>   <b>Oral solution: 400mg lopinavir/ 100mg ritonavir per 5mL</b></p>	<p>3 capsules (400mg lopinavir + 100mg ritonavir) BID                   4 capsules BID if used with efavirenz or nevirapine in treatment-experienced pts where reduced lopinavir susceptibility is suspected</p>	<p>Not necessary</p>	<p>For both capsules &amp; liquid                   Pharmacy store in refrigerator until dispense                   For patients, if stored in room temperature, discard after two months</p>	<p><b>ritonavir</b>                  Take with food.                   Take one hr before or two hr after ddI.                   Oral solution contains 42.4% alcohol</p>
<p><b>Nelfinavir (Viracept<sup>®</sup>)</b>                  Light blue capsule-shaped tab 250mg.  <b>Oral powder:</b> 50 mg of nelfinavir/Gm (scoop)</p>	<p>750 mg TID (9 tab/day) or 1250 mg BID (10 tab/d)</p>	<p>Not Necessary                   Hemodialysis - Not likely to affect clearance</p>	<p>Room temperature   <b>Oral powder</b> - once mixed with liquid, use within 6 hours</p>	<p>Take with food or light snack</p>
<p><b>Ritonavir (Norvir<sup>®</sup>)</b>                  off white soft gel cap - 100 mg   <b>Oral solution-</b> 600mg/7.5 ml</p>	<p>600 mg (7.5cc) BID (titration from 300-400 mg BID to full dose in &lt; 2 wks; total 12 cap/day);</p>	<p>Not Necessary                   Hemodialysis - not likely to affect clearance</p>	<p><b>Oral Capsules</b> - Refrigerate - discard if left at room temp for &gt; 30 days  <b>Oral Solution</b> – Do Not Refrigerate; Advise pt not to use pass expiration date on bottle.</p>	<p>With meals if possible                   At least 2.5hr apart from ddI.                   Oral solution can be taken w/ Ensure, chocolate milk or Advera</p>
<p><b>Saquinavir Soft Gel Cap (Fortovase<sup>®</sup>)</b>                  Beige, opaque, soft gelatin capsule - 200 mg   <b>Hard Gel Cap (Invirase<sup>®</sup>)</b>                  Yellow &amp; green cap – 200mg</p>	<p><b>Fortovase: As single PI</b> 1200mg TID (18 cap/day)   <b>Invirase:</b> As single PI - 600 mg TID (9 cap/day) – Not Recommended   <b>NOT RECOMMENDED TO BE USED AS SINGLE PI IN PRESENCE OF EFAVIRENZ</b></p>	<p>Not necessary                   Hemodialysis - not likely to affect clearance</p>	<p><b>Fortovase: Pharmacy - refrigerate before dispensing.</b>   <b>If left refrigerated</b>- good until company’s expiration date  <b>At room temp</b>- discard after 3 months   <b>Invirase:</b> Room Temperature</p>	<p>Take with a meal or at up to 2 hours after a meal</p>

Prepared by A.Pau, Pharm.D. (NIH CC Pharmacy Dept, Clinical Pharmacy Specialist for NIAID) 4/97; Revised 5/97; 7/97; 11/97; 5/98; 9/98; 12/98; 4/99; 7/99. 11/99; 2/00; 5/00; 9/00 . Please refer to Combination Dosage Modification table for dosage adjustments when combination therapy is use