

Appendix: Alternative Protease Inhibitors for Patients Discontinuing Viracept

In all cases, consideration should be given to what other medications the patient is taking to avoid negative drug-drug interactions that may not have been an issue when the patient was receiving Viracept. If the patient is switched to a ritonavir containing regimen the product label for ritonavir (Norvir) should also be consulted and drug-drug interactions associated with the inhibition of Cytochrome P450 3A4 by ritonavir taken into account.

Each protease inhibitor has different characteristics with regards to factors such as taking with food, use in special populations (for example, people with liver disease) and especially drug-drug interactions with other antiretrovirals or other medications taken concomitantly. These factors should be evaluated and the product label of the new drug should be consulted when switching the patient to a new protease inhibitor.

Additional resources that will guide the selection of alternative protease inhibitors includes the US Dept of Health and Human Services Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents, Oct. 10, 2006 (<http://AIDSinfo.nih.gov>).

Alternative Protease Inhibitors

Protease inhibitor (PI)	Posology	Predicted activity in patients virologically suppressed with Viracept	Paediatric indication/ formulation available	Special patient populations who may be excluded from PI
Kaletra (lopinavir/r)	400mg lopinavir/100mg ritonavir (co-formulated) twice daily	Yes	Yes > 6 months/ Yes	Generally well tolerated in mild to moderate renal and liver impairment. Caution is warranted in patients with severe renal impairment. Recommended not to be given in patients with severe liver impairment. Can be used in pregnancy ONLY if clearly necessary (risks unknown but evidence of reproductive toxicity exists).
Invirase (saquinavir/r)	1000mg saquinavir with 100mg ritonavir twice	Yes	No/No	Generally well tolerated in mild to moderate renal and liver impairment. Contraindicated in severe liver

	daily with food			impairment. Can be used in pregnancy if benefits outweigh risks.
Reyataz (atazanavir/r)	300mg atazanavir with 100mg ritonavir once daily. (Data available for 400mg once daily taken without ritonavir/unboosted, although this dose is only approved in a few countries)	Yes if given in combination with ritonavir. (For unboosted atazanavir, antiviral activity is expected, yet prior treatment history needs to be taken into account and patients should be monitored closely for treatment response) No benefit if ≥ 4 PI mutations	No/No (risk of kernicterus in infants < 3 mo. old.)	Generally well tolerated in renal impairment. Should be used with caution in patients with mild liver insufficiency. Should not be used in patients with moderate to severe liver insufficiency.
Telzir (fosamprenavir/r)	700 mg fosamprenavir with 100 mg ritonavir twice daily with or without food. (Data available for 1400 mg twice daily taken without ritonavir/unboosted, although this dose is only approved in few countries)	Yes if given in combination with ritonavir. (For unboosted fosamprenavir antiviral activity is expected, yet prior treatment history needs to be taken into account and patients should be monitored closely for treatment response)	No/No	Limited data in the elderly. Generally well tolerated in renal impairment. Should be used with caution in patients with mild or moderate liver impairment and is contraindicated in patients with severe liver impairment. Insufficient data to recommend in pregnancy.
Prezista	600 mg darunavir	Yes	No/No	Limited data in the elderly. Should be used

(darunavir/r)	with 100 ritonavir twice daily			with caution in patients with mild or moderate liver impairment (Child-Pugh Class A and B) and should not be used in patients with sever liver impairment (Child-Pugh Class C). Okay in renal impairment. Insufficient data to recommend in pregnancy.
Aptivus (tipranavir/r)	500mg tipranavir with 200mg ritonavir twice daily.	Yes	No/No	Should be used with caution in patients with mild liver impairment (Child-Pugh Class A) and should not be used in patients with moderate to sever liver impairment (Child-Pugh Class B or C). Insufficient data to recommend in pregnancy.
Crixivan (indinavir)	800 mg every 8 hours (Data available for Indinavir given with ritonavir, but not approved for in this combination)	Yes	Optimal dosing in pediatrics not established/No	Increased indirect hyperbilirubinemia. Dosage adjustment for patients with liver insufficiency due to cirrhosis. Ritonavir boosted indinavir an alternate agent in pregnancy; optimal dosing unknown.