Table 10: one of two pages

Table 10. Advantages and Disadvantages of Different Protease Inhibitors (PIs) for Use in Highly Active Antiretroviral Combination Regimens

	Advantages	Disadvantages
General Issues		
Protease Inhibitor-Based Regimens	**Protease Class Advantages:** • NNRTI-sparing • Clinical, virologic and immunologic efficacy well-documented • Resistance to protease inhibitors requires multiple mutations • Targets HIV at 2 steps of viral replication (viral reverse transcriptase and protease enzymes)	**Protease Class Disadvantages:** • Metabolic complications including dyslipidemia, fat maldistribution, insulin resistance • Potential for multiple drug interactions due to metabolism via hepatic enzymes (e.g. CYP3A4) • Higher pill burden than NRTI or NNRTI-based regimens for those taking solid formulations • Poor palatability of liquid preparations, which may affect adherence to treatment regimen
Strongly Recommended		
Lopinavir/ ritonavir	• Coformulated liquid and capsule formulations • Can give with food	• Poor palatability of liquid (bitter taste), although better than ritonavir alone • Food effect (should be administered with food) • Ritonavir component associated with large number of drug interactions (see ritonavir)
Nelfinavir	• Powder formation (for liquid preparation) • Few adverse effects • Can give with food	• Diarrhea • Powder formulation poorly tolerated • Food effect (should be administered with food) • Appropriate dosage for younger children not well-defined • Need for 3-times daily dosing for younger children
Ritonavir	• Liquid formulation • Can give with food	• Poor palatability of liquid (bitter taste) • Gastrointestinal intolerance • Food effect (should be administered with food) • Largest number drug interactions (most potent inhibitor of CYP3A4)
Alternative		
Indinavir		• Only available in capsule • Possible higher incidence nephrotoxicity in children • Requires 3-times daily dosing • High fluid intake required • Food effect (should be taken 1 hour before or 2 hours after food) • Lack of pediatric pharmacokinetic data
Amprenavir	• Can give with food	• Poor palatability of liquid (bitter taste) • Due to potential toxicity from high amounts of propylene glycol in oral solution, cannot use in children <4 years • Skin rash • Large volume of liquid formulation required

Table 10: two of two pages

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Insufficient Data to Recommend		
Fosamprenavir	• Oral prodrug of amprenavir with lower pill burden • Can give with food	• Skin rash
Saquinavir soft-gel capsule		• Should not be used as sole protease inhibitor in children • Limited information on appropriate dosing in children; will require boosting with another protease inhibitor (e.g., ritonavir) to achieve adequate concentrations, but pharmacokinetic data in children on appropriate dosing of combination not available • Only available in capsule • High pill burden • Must be taken with food • Photosensitivity reactions can occur
Saquinavir hard-gel capsule		• Should not be used as sole protease inhibitor in children • Limited information on appropriate dosing in children; will require boosting with another protease inhibitor (e.g., ritonavir) to achieve adequate concentrations, but pharmacokinetic data in children on appropriate dosing of combination not available • Only available in capsule • High pill burden • Poor bioavailability; must be taken with food
Atazanavir	• Once daily dosing (adults) • Minimal effect on triglyceride and total cholesterol levels than other protease inhibitors (adults)	• No data on pediatric dosing or safety • No liquid formulation • Food effect (should be administered with food) • Indirect hyperbilirubinemia common but asymptomatic • Use in caution in patients with pre-existing conduction system defects (can prolong PR interval of electrocardiogram)