



Florida/Caribbean AIDS Education and Training Center

# HIV CareLink

A Newsletter for HIV/AIDS Primary Care Providers

## ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides state-of-the-art HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

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## Special Bulletin: Use of Antiretroviral Agents in Pediatric Infection Guidelines

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The Panel on Antiretroviral Therapy and Medical Management of HIV-infected Children has updated the *Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*. These guidelines address issues specific to the use of antiretroviral therapy (ART) for HIV-infected infants, children, and adolescents and include revised information on when to start ART as well as the management of adverse events of antiretroviral (ARV) drugs in children in the following areas: central nervous system (CNS) toxicity, gastrointestinal effects (GI), nephrotoxic effects, and peripheral nervous system toxicity. A concise summary is included. Clinicians are encouraged to consult the full Guidelines at <http://www.aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf> for details.

### Diagnosis of HIV Infection in Infants

- Similar recommendations continue for testing HIV-exposed infants at age 14-21 days, 1-2 months and 4-6 months, by viral diagnostic testing and include consideration for testing at birth for infants at high risk for infection. Both HIV DNA and HIV RNA testing are recommended; however, consideration for HIV RNA testing with one of the newer assays is preferred if non-subtype B HIV is suspected (See Guidelines for detailed discussion).
- Some experts would repeat virologic testing if the confirmatory HIV antibody test is positive at 18 months of age (possible late seroreverter, as late as 24 months of age). There have been rare cases of late postnatal diagnoses despite negative virologic tests through 6 months of age and infants infected with non-subtype B HIV may have false negative HIV DNA PCR results.

**When to Initiate Antiretroviral Therapy:** See table on page 3

### Factors to Consider When Selecting an Initial Regimen

- Providers should individualize ARV regimen based on characteristics of the proposed regimen, complexity of schedules, formulations, patient characteristics, and resistance testing results. New once daily dosing information is available for selected therapy.

### What ARVs to Start-Initial Therapy

- For all infants and children ages  $\geq 14$  days to  $< 3$  years, the preferred initial therapy is lopinavir/ritonavir plus two alternative

regimen nucleoside reverse transcriptase inhibitors (NRTIs). According to new data on cardiovascular toxicity in preterm infants, lopinavir/ritonavir should not be used in neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days.

- Nevirapine-based regimens are now considered an alternative for initial therapy for infants and children ages  $\geq 14$  days to  $< 3$  years.
- Efavirenz plus 2 NRTIs remains a preferred option for children  $\geq 3$  years of age.
- In children ages  $\geq 6$  years, ritonavir-boosted atazanavir was added as a second preferred PI option.
- The new NNRTI rilpivirine is not recommended for initial therapy in children because of lack of data in pediatric patients and lack of pediatric formulation.
- For initial therapy the preferred dual-NRTI backbone regimens include:
  - Age  $\geq 3$  months: abacavir plus lamivudine or emtricitabine
  - Age  $\geq 12$  years and Tanner Stage 4 or 5: tenofovir plus lamivudine or emtricitabine, or
  - Any age: zidovudine plus lamivudine or emtricitabine.
- Alternative dual-NRTI backbone regimens for initial therapy have been added:
  - Any age: didanosine plus lamivudine or emtricitabine, or
  - Age  $\geq 12$  years and Tanner Stage 3 or, in special circumstances, for adolescents age  $\geq 12$  years and Tanner Stage 2: tenofovir plus lamivudine or emtricitabine.

For more information,  
please visit our website:

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To request clinical consultation, please call the  
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### Choice of NNRTI vs. PI-Based Initial Regimens

- A PI-based regimen containing lopinavir/ritonavir is considered the preferred initial regimen for children <3 years of age based on superior virologic suppression seen in the P1060 study. A nevirapine-containing regimen remains an acceptable alternative for infants not exposed to single-dose nevirapine for prevention of mother-to-child transmission if the infant cannot tolerate lopinavir/ritonavir.
- Either an NNRTI-based or a PI-based regimen is acceptable in children >3 years of age.

### Monitoring

- “Blips” (temporary viral load elevations between the level of detection and 1,000 copies/mL) can be seen in children and adults and should not be considered evidence of virologic failure.
- A new recommendation to perform urinalysis (U/A) at baseline and every 6–12 months has been added.

### Toxicity

- New sections added to Table 17 include: Antiretroviral Therapy-Associated Adverse Effects and Management Recommendations, on 1.) CNS toxicity, 2.) GI effects, 3.) nephrotoxicity, and 4.) peripheral nervous system toxicity. Existing sections have been updated.

### Treatment Failure

- A new section has been added which discusses management of children with ongoing adherence problems as the reason for viral failure.
- The use of lamivudine or emtricitabine monotherapy as an interim “bridging regimen” in children with treatment failure associated with drug resistance and ongoing non-adherence is discussed as a potential option.

### Resistance Testing

- Genotypic assays to detect mutations associated with CXCR4 or D/M tropic virus (Tprofile-DNA) are discussed and can be used to determine the possible utility of a CCR5 inhibitor in patients with undetectable viral loads that preclude use of standard tropism testing.

### Pediatric Antiretroviral Drug Information

The section has been reorganized; updates with new pediatric data are provided for specific drugs.

- Abacavir: Once-daily abacavir dosing (16 mg/kg/day, maximum 600 mg once daily) in clinically stable children with undetectable viral load and stable CD4 count.
- Lamivudine: Once-daily lamivudine (300 mg once daily) for adolescents age ≥16 years who weigh ≥50 kg.

- Stavudine: 30 mg twice daily regardless of weight recommended in adults and older adolescents.
- Tenofovir: Updated information on the effect of tenofovir on bone mineral density (BMD) and renal function in children.
- Efavirenz: Consideration for the use of therapeutic drug monitoring (TDM) in the setting of efavirenz-related toxicity is discussed due to interpatient variability in drug exposure secondary to polymorphisms in cytochrome P (CYP) 450 genes.
- Etravirine: Pediatric investigational dosing for etravirine in children ≥6 years of age: 5.2 mg/kg (maximum 200 mg) twice daily (currently being investigated in Phase II trial)
- Nevirapine: Extended-release nevirapine is newly available for adults, but not approved in children age <18 years due to lack of data in this age group.
- Rilpivirine: Drug information on rilpivirine is added; however, no pediatric data is available.
- Darunavir: Once-daily dosing (darunavir 800 mg plus ritonavir 100 mg) may be considered for treatment-naïve pediatric patients age 12–18 years who weigh >40 kg. Once-daily darunavir dosing is not recommended for any children age <12 years or <18 years if treatment-experienced.
- Saquinavir: Significant PR and QT prolongation has been seen. Perform electrocardiogram (ECG) prior to use and do not use in individuals with prolonged QT interval or those receiving other drugs that may prolong the QT interval.

## Keeping with the Pace 2011: An HIV/AIDS Update

Wednesday, August 31, 2011  
12:30 PM - 4:45 PM

Available LIVE online via web video conferencing!

OR on-site:

Best Western Gateway Grand - Gainesville, Florida  
Check-in for on-site participants begins at 11:45 AM

### PRESENTED BY

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Training Agenda and Registration:

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**When to Initiate Antiretroviral Therapy**

Age	Clinical Category		CD4+ cell percentage or count		Plasma HIV RNA (copies/mL)	RECOMMENDATION
<12 months	ALL		ANY VALUE		ANY VALUE	Treat regardless of clinical symptoms, immune status, or viral load (AI)
1<5y	AIDS or significant HIV-related symptoms <sup>1</sup>		ANY VALUE		ANY VALUE	TREAT (AI*) <sup>4</sup>
	All categories	and	<25%	and	ANY VALUE	TREAT (AII)
	Asymptomatic or mild symptoms* <sup>2</sup>	and	≥25%	and	≥100,000	TREAT (BII)
	Asymptomatic or mild symptoms* <sup>2</sup>	and	≥25%	and	<100,000	Consider treatment <sup>3</sup> (CIII)
≥5 y	AIDS or significant HIV-related symptoms <sup>1</sup>		ANY VALUE		ANY VALUE	TREAT (AI*) <sup>4</sup>
	All categories	and	≤500 cells/mm <sup>3</sup>		ANY VALUE	TREAT: CD4 count <350 cells/mm <sup>3</sup> (AI*) <sup>4</sup> CD4 count 350-500 cells/mm <sup>3</sup> (BII*) <sup>5</sup>
	Asymptomatic or mild symptoms <sup>2</sup>	and	>500 cells/mm <sup>3</sup>	and	≥100,000	TREAT (BII*) <sup>5</sup>
	Asymptomatic or mild symptoms <sup>2</sup>	and	>500 cells/mm <sup>3</sup>	and	<100,000	Consider treatment <sup>3</sup> (CIII)

1. CDC Clinical Categories C and B except for: single episode of serious bacterial infection (Category B condition)
  2. CDC Clinical Category A or N or single episode of serious bacterial infection (Category B condition)
  3. Re-evaluate clinical and laboratory data every 3 to 4 months
  4. I\*: One or more randomized trials in adults with clinical outcomes and/or validated laboratory endpoints with accompanying data in children<sup>†</sup> from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes
  5. II\*: One or more well-designed, nonrandomized trials or observational cohort studies in adults with long-term clinical outcomes with accompanying data in children<sup>†</sup> from one or more smaller nonrandomized trials or cohort studies with clinical outcome data
- <sup>†</sup> Studies that include children or children/adolescents but not studies limited to postpubertal adolescents

**References**

1. Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. August 11, 2011; pp 1-268. Available at <http://aidsinfo.nih.gov/ContentFiles/PediatricGuidelines.pdf>. Accessed (08-12-2011) [pgs. I-iii; 12-13; 45; 143]

**6th IAS Conference on HIV Pathogenesis, Treatment and Prevention**

The world's largest open scientific conference on HIV/AIDS – the 6th IAS Conference on HIV Pathogenesis, Treatment and Prevention, held in Rome Italy in July 2011, was organized by the IAS in partnership with Istituto Superiore di Sanità (Italian National Institute of Health), the leading technical and scientific body of the Italian National Health Service.

Held every two years, the conference attracts nearly 5,000 delegates from around the world. The event is a unique opportunity for the world's leading scientists, clinicians, public health experts and community leaders to examine the latest developments in HIV-related research.

To view Capsule Summaries of the 2011 IAS Conference, visit the Clinical Care Options HIV website:  
<http://www.clinicaloptions.com/HIV/Conference%20Coverage/Rome%202011.aspx>

For a downloadable slide set of the conference coverage, visit this link:  
[http://www.clinicaloptions.com/HIV/Conference%20Coverage/Rome%202011/CCO%20Slideset/Highlights\\_Slideset.aspx](http://www.clinicaloptions.com/HIV/Conference%20Coverage/Rome%202011/CCO%20Slideset/Highlights_Slideset.aspx)

To view sessions and abstracts from the 6<sup>th</sup> IAS Conference on HIV Pathogenesis, Treatment and Prevention (July 2011), visit this link:  
<http://pag.ias2011.org/>

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### Complera™ (emtricitabine/rilpivirine/tenofovir DF)

The fixed dose combination (FDC) drug Complera™ (emtricitabine/rilpivirine/tenofovir DF) was FDA approved for the treatment of HIV 1 on August 10, 2011.

- Recommended dosing of emtricitabine/rilpivirine/tenofovir DF FDC (200mg/25mg/300mg) is one tablet, once daily, taken orally with a meal.
- Approved for use in ARV treatment naïve adult patients.
- Rilpivirine treated patients with higher HIV viral loads (>100,000 copies/mL) at the start of therapy had a higher rate of virologic failure in clinical trials when compared to those with a lower HIV viral load (<100,000 copies/mL) at start of therapy.
- Rilpivirine treated patients had a higher rate of overall treatment resistance and cross-resistance to the NNRTI class as compared to efavirenz treated patients in clinical trials.
- Rilpivirine treated patients had a higher rate of lamivudine/emtricitabine associated resistance compared to efavirenz treated patients in clinical trials.
- Multiple contraindications exist with concomitant medications i.e. anticonvulsants, antimycobacterials, proton pump inhibitors, dexamethasone, and St. Johns wort.
- On 8/16/11, the DHHS Adult and Adolescent Antiretroviral Treatment Guidelines Panel classified Rilpivirine as an alternative NNRTI (BI) for initial therapy. Alternative regimen = regimen that is effective and tolerable but has potential disadvantages compared with preferred regimens. An alternative regimen may be the preferred regimen for some patients. BI rating=Moderate recommendation for the statement, one or more randomized trials with clinical outcomes and/or validated laboratory endpoints.

#### References

1. FDA Approves Rilpivirine (Edurant™) for Treatment-Naïve Patients, F/C AETC CareLink #7, June 22, 2011. [http://www.faetc.org/PDF/Newsletter/Newsletter-Volume12-2011/HIVCareLink-06-22-11-v12\\_i07-Rilpivirine.pdf](http://www.faetc.org/PDF/Newsletter/Newsletter-Volume12-2011/HIVCareLink-06-22-11-v12_i07-Rilpivirine.pdf)
2. Approval of Complera: emtricitabine/rilpivirine/tenofovir DF fixed dose combination. <http://www.fda.gov/ForConsumers/ByAudience/ForPatientAdvocates/HIVandAIDSactivities/ucm267592.htm>
3. DHHS Adult and Adolescent Antiretroviral Treatment Guidelines Panel Releases Supplemental Information Regarding the Role of Rilpivirine as Initial Therapy, Issue No. 35, August 16, 2011. <http://aidsinfo.nih.gov/ListServ/PreviewPage.aspx?pageID=461>



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