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SPECIAL BULLETIN

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Adult and Adolescent Antiretroviral Guidelines Updated January 29, 2008

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The Department of Health and Human Services (DHHS) released an update of the Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents on January 29, 2008. This updates the Guidelines from the previous version dated December 1, 2007. This edition of *HIV CareLink* summarizes the major changes to the Guidelines. The clinician is encouraged to consult the full set of Guidelines online at <http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf>.

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ABOUT US

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

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THERAPY IN ARV-NAÏVE PATIENTS

Changes to Table of Preferred and Alternative Antiretroviral Components (see table on next page)

- Abacavir + lamivudine (ABC/3TC available as Epzicom[®]) changed from "alternative" to "preferred" NRTI components in patients testing negative for HLA-B*5701
- Zidovudine + lamivudine (available as Combivir[®]) changed from "preferred" to "alternative" NRTI components
 - Rationale: adverse effects such as anemia, mitochondrial toxicity, inferior to tenofovir/emtricitabine (TDF/FTC) when each combined with efavirenz (EFV), less CD4 cell count ↑ compared to ABC/3TC, greater selection of M184V compared to TDF/FTC
- Ritonavir (RTV)-boosted saquinavir (Invirase[®]) changed from a PI option that was considered an "Acceptable as initial antiretroviral components but inferior to preferred or alternative components" to "alternative" PI component
- No longer recommended as components for initial therapy in treatment-naïve patients:
 - Nelfinavir (Viracept[®])
 - Stavudine (Zerit[®]) + lamivudine (EpiVir[®]) as NRTI components
 - Abacavir + zidovudine + lamivudine (Trizivir[®]) as 3-NRTI combination regimen

• New Topic: "Other Treatment Options Under Investigation: Insufficient Data to Recommend"

- RTV-boosted darunavir (DRV, Prezista[™]): discussion of ARTEMIS study which compared DRV 800 mg/RTV 100 mg qd with lopinavir/RTV (Kaletra[®]) qd or bid; significantly more DRV/RTV-treated patients achieved VL < 50 copies/mL (84% vs. 78%, p < 0.001); not yet recommended since data preliminary and 400 mg DRV tablet not yet available
- Raltegravir (Isentress[™])-based regimen: 24 week analysis of Phase II dose-ranging study showed similar # of patients achieved VL < 50 copies/mL with all doses of raltegravir compared to EFV-based regimen; durable activity seen at 48 week analysis; Phase III studies in ARV-naïve patients ongoing
- Maraviroc (MVC, Selzentry[™])-based regimen: patients with R5 virus only enrolled in MERIT study comparing MVC-based regimen to EFV-based regimen; non-inferiority of MVC vs. EFV not shown for HIV RNA < 50 copies/mL endpoint; more MVC patients discontinued study due to lack efficacy; CD4 ↑ 170 and 153 cells/mm³ with MVC and EFV, respectively

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TREATMENT INTERRUPTION

- Updated with new information on short-term and long-term treatment interruption
- Recommendation remains that long-term treatment interruptions are not recommended except in the context of a clinical trial

ACUTE HIV INFECTION

- New table on identifying, diagnosing, and managing acute HIV infection replaces prior table that listed signs and symptoms and expected frequency
- Recommendation that since baseline NNRTI resistance is more common than PI resistance in ARV-naïve patients, a PI-based regimen should be considered in patients for whom therapy is initiated before resistance test results available

ACTIVE TB DISEASE OR LATENT TB IN HIV COINFECTION

- Discussion regarding timing of initiation of ART in patients who require treatment of active TB; Note: presence of active TB requires immediate initiation of treatment for active TB
- Consider delaying initiation of ART in ARV-naïve patients until a period of time *after* initiation of active TB therapy to better distinguish adverse drug reactions and to ↓ risk of Immune Reconstitution Inflammatory Syndrome (IRIS)
- Some experts base timing of ART initiation on CD4 cell count:
 - < 100: start ART 2 weeks *after initiation* of TB treatment
 - 100-200: start ART 8 weeks *after initiation* of TB treatment
 - 200-350: start ART 8 weeks *after initiation* of TB treatment on a case by case basis with clinician's judgment
 - > 350: start ART 8-24 weeks *after completion* of TB treatment on a case by case basis with clinician's judgment

- Management of IRIS
 - Optimal management unknown
 - Continue treatment for both TB and HIV
 - Consider NSAIDs for mild cases or high dose corticosteroids for 1-4 weeks for severe cases (length of treatment and need to taper based on control of symptoms)
- Rifabutin is the preferred rifamycin in HIV co-infected patients due to less drug interactions with ARVs
- Recommendation for repeat testing for latent TB infection in patients who had a negative test when CD4 < 200 cells/mm³ and whose CD4 has increased to > 200 cells/mm³

TABLE UPDATES

Various tables updated, some selected highlights below:

- Information regarding new NNRTI etravirine (ETV, Intelence™) added to various tables (see recent [HIV Carelink](#) for information about ETV); since etravirine + 2 NRTIs underperformed in comparison to a PI-based regimen in ARV-experienced patients who failed a prior NNRTI-based regimen, the DHHS Panel recommends that this agent not be used with 2 NRTIs without addition of another active agent [e.g. a selected boosted PI (due to drug interactions, *cannot* combine ETV with all boosted PIs)]
- Updated information regarding drug interaction between proton pump inhibitors and the PI atazanavir (ATV, Reyataz®)
 - Can use RTV-boosted ATV with proton pump inhibitor (equivalent of omeprazole 20 mg once daily) in *treatment-naïve patients only* taken at least 12 hours prior to atazanavir/ritonavir. [Reyataz® label](#) recently updated with this information. Note: ATV levels still ↓ (ratio of ATV C_{min} with/ without omeprazole 20 mg daily = 0.54).

(Adapted from Table 6: Antiretroviral Components Recommended for Treatment of HIV-1 Infection in Treatment-Naïve Patients)

To Construct an ARV Regimen, Select 1 Component from Column A and 1 Component from Column B

Column A (NNRTI or PI Options in Alphabetical Order)		OR	Column B (Dual-NRTI Options)	
Preferred Components	NNRTI		PI	Preferred Components (alphabetical order)
	efavirenz ¹		atazanavir + ritonavir fosamprenavir + ritonavir (bid) lopinavir + ritonavir (bid) ²	abacavir/lamivudine ³ (Epzicom®) for patients who test negative for HLA-B*5701 or tenofovir/emtricitabine (Truvada®)
Alternatives to Preferred Components	nevirapine ⁴		atazanavir ⁵ fosamprenavir fosamprenavir + ritonavir (qd) lopinavir/ritonavir (qd) saquinavir + ritonavir	Alternatives to Preferred Components (order of preference)

1. Efavirenz not recommended in 1st trimester of pregnancy or in sexually active women with childbearing potential who are not using adequate contraception.
2. Pivotal study leading to recommendation of lopinavir/ritonavir as preferred PI based on bid dosing; smaller study has shown similar efficacy with qd dosing but with more GI adverse effects and potentially insufficient response with qd dosing in patients with HIV RNA > 100,000 copies/mL.
3. Emtricitabine may be used in replace of lamivudine and vice versa (potential for use of coformulation is major determining factor).
4. Nevirapine should not be initiated in ART-naïve women with CD4 > 250 and ART-naïve men with CD4 > 400 cells/mm³ due to risk of symptomatic hepatic events.
5. Atazanavir must be boosted with ritonavir if used with tenofovir or efavirenz.

Reference:

1. Panel on Antiretroviral Guidelines for Adult and Adolescents. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. Department of Health and Human Services. January 29, 2008. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. (Accessed January 30, 2008)

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