Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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Introduction (Last updated February 12, 2013; last reviewed February 12, 2013)

Antiretroviral therapy (ART) for the treatment of HIV infection has improved steadily since the advent of potent combination therapy in 1996. New drugs that offer new mechanisms of action, improvements in potency and activity even against multidrug-resistant viruses, dosing convenience, and tolerability have been approved. ART has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV disease into a chronic, manageable condition. In addition, effective treatment of HIV-infected individuals with ART is highly effective at preventing transmission to sexual partners.[1] However, less than one-third of HIV-infected individuals in the United States have suppressed viral loads,[2] which is mostly a result of undiagnosed HIV infection and failure to link or retain diagnosed patients in care. Despite remarkable improvements in HIV treatment and prevention, economic and social barriers that result in continued morbidity, mortality, and new HIV infections persist.

The Department of Health and Human Services (HHS) Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) is a working group of the Office of AIDS Research Advisory Council (OARAC). The primary goal of the Panel is to provide HIV care practitioners with recommendations based on current knowledge of antiretroviral (ARV) drugs used to treat adults and adolescents with HIV infection in the United States. The Panel reviews new evidence and updates recommendations in these guidelines when needed. The Panel's primary areas of attention have included baseline assessment, treatment goals, indications for initiation of ART, choice of the initial regimen for ART-naive patients, drugs or combinations to avoid, management of adverse effects and drug interactions, management of treatment failure, and special ART-related considerations in specific patient populations. For recommendations related to pre-exposure HIV prophylaxis (PrEP) for HIV-uninfected persons, please refer to recommendations from the Centers for Disease Control and Prevention (CDC).[3, 4]

These guidelines generally represent the state of knowledge regarding the use of ARV agents. However, because the science of HIV evolves rapidly, the availability of new agents and new clinical data may change therapeutic options and preferences. Information included in these guidelines may not be consistent with approved labeling for the particular products or indications in question, and the use of the terms "safe" and "effective" may not be synonymous with the Food and Drug Administration (FDA)-defined legal standards for product approval. The Panel frequently updates the guidelines (current and archived versions of the guidelines are available on the AIDS*info* website at http://www.aidsinfo.nih.gov). However, the guidelines cannot always be updated apace with the rapid evolution of new data in the field of HIV and cannot offer guidance on care for all patients. Clinicians should exercise clinical judgment in management decisions tailored to unique patient circumstances.

The Panel recognizes the importance of clinical research in generating evidence to address unanswered questions related to the optimal safety and efficacy of ART. The Panel encourages both the development of protocols and patient participation in well-designed, Institutional Review Board (IRB)-approved clinical trials.

Guidelines Development Process

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the guidelines	Provide guidance to HIV care practitioners on the optimal use of antiretroviral (ARV) agents for the treatment of HIV infection in adults and adolescents in the United States.
Panel members	The Panel is composed of approximately 40 voting members who have expertise in HIV care and research. The Panel includes at least one representative from each of the following U.S. Department of Health and Human Services (HHS) agencies: Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Health Resource Services Administration (HRSA), and National Institutes of Health (NIH). Approximately two-thirds of the Panel members are non-governmental scientific members. The Panel also includes four to five community members with knowledge in HIV treatment and care. The U.S. government representatives are appointed by their respective agencies; other Panel members are selected after an open announcement to call for nominations. Each member serves on the Panel for a 4-year term with an option for reappointment for an additional term. A list of current members can be found in the Panel Roster.
Financial disclosure	All members of the Panel submit financial disclosure in writing annually, reporting any association with manufacturers of ARV drugs or diagnostics used for management of HIV infections. A list of the latest disclosures is available on the AIDS*info* website (http://aidsinfo.nih.gov/contentfiles/AA_financialDisclosures.pdf).
Users of the guidelines	HIV treatment providers
Developer	Panel on Antiretroviral Guidelines for Adults and Adolescents—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding source	Office of AIDS Research, NIH
Evidence collection	The recommendations in the guidelines are generally based on studies published in peer-reviewed journals. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation grading	As described in Table 2
Method of synthesizing data	Each section of the guidelines is assigned to a working group of Panel members with expertise in the area of interest. The working groups synthesize the available data and propose recommendations to the Panel. The Panel discusses all proposals during monthly teleconferences. Recommendations endorsed by the Panel are included in the guidelines as official recommendations.
Other guidelines	These guidelines focus on treatment for HIV-infected adults and adolescents. Included is a brief discussion on the management of women of reproductive age and pregnant women. For more detailed and up-to-date discussion on the use of antiretroviral therapy (ART) for these women, as well as for children, and other special populations, please refer to guidelines specific to these groups. The guidelines are also available on the AIDS*info* website (http://www.aidsinfo.nih.gov).
Update plan	The Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, dosing formulations, or frequency of dosing), new significant safety or efficacy data, or other information that may have a significant impact on the clinical care of patients. In the event of significant new data that may affect patient safety, the Panel may post a warning announcement with recommendations on the AIDS*info* website in the interim until the guidelines can be updated with the appropriate changes. Updated guidelines are available on the AIDS*info* website (http://www.aidsinfo.nih.gov).
Public comments	A 2-week public comment period follows release of the updated guidelines on the AIDS*info* website. The Panel reviews comments received to determine whether additional revisions to the guidelines are indicated. The public may also submit comments to the Panel at any time at contactus@aidsinfo.nih.gov.

Basis for Recommendations

Recommendations in these guidelines are based upon scientific evidence and expert opinion. Each recommended statement includes a letter (**A**, **B**, or **C**) that represents the strength of the recommendation and with a Roman numeral (**I**, **II**, or **III**) that represents the quality of the evidence that supports the recommendation (see Table 2).

Table 2. Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement	**I:** One or more randomized trials with clinical outcomes and/or validated laboratory endpoints
B: Moderate recommendation for the statement	**II:** One or more well-designed, non-randomized trials or observational cohort studies with long-term clinical outcomes
C: Optional recommendation for the statement	**III:** Expert opinion

HIV Expertise in Clinical Care

Many studies have demonstrated that outcomes achieved in HIV-infected outpatients are better when care is delivered by a clinician with HIV expertise,[5-10] which reflects the complexity of HIV infection and its treatment. Thus, appropriate training and experience, as well as ongoing continuing education, are important components of optimal care. Primary care providers without HIV experience, such as those who provide service in rural or underserved areas, should identify experts in their regions who will be available for consultation when needed.

References

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