



Antiretroviral drugs and the prevention of mother-to-child transmission of HIV infection in resource-limited settings

Recommendations for a Public Health Approach (2005 Revision)

Geneva, Switzerland
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Important new evidence has become available regarding more potent antiretroviral regimens to prevent mother-to-child transmission of HIV (MTCT), safety of Highly Active Antiretroviral Therapy (HAART) in pregnant women and resistance following single-dose nevirapine among mothers and its implications for their future treatment options. WHO convened a Technical Consultation in Geneva, Switzerland on 28-29 June 2005 to review the new information and update the *Guidelines on the use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants*. The Consultation considered the need to harmonise these guidelines with the adult and paediatric HIV-treatment guidelines, and to simplify them to facilitate implementation at country level.

Several factors related to the health system and to patients can hinder the uptake of interventions for the prevention of MTCT (PMTCT) and the quality of services provided. These include the strength of health service infrastructure, the availability of financial and human resources, access to and use of health services such as antenatal care services, and the proportion of deliveries attended by a skilled health care worker. Socio-cultural factors and individual circumstances and conditions also influence the uptake and quality of services provided. While the full PMTCT interventions can be delivered in well-resourced health facilities, the group recognised that in order to expand coverage and ensure that the largest number of women and their infants benefit, simple and effective PMTCT interventions can and must be delivered in settings with limited capacity. In addition, the selection of antiretroviral regimens must be adapted to specific circumstances, for example women who first present for antenatal care late in pregnancy or only around delivery or with particular conditions such as co-infection with tuberculosis.

The Technical Consultation reviewed the most recent information and programmatic experience with implementing PMTCT interventions and the recommendations from the 2004 guidelines. In making its recommendations the Technical Consultation considered seven overarching principles:

- a) WHO promotes a comprehensive strategic approach to the prevention of HIV infection in infants which includes: (1) primary prevention of HIV infection; (2) prevention of unintended pregnancies among HIV-infected women; (3) prevention of HIV transmission from HIV-infected mothers to their infants; and (4) care treatment and support for HIV-infected mothers and their children. While the participants recognised the importance of all the four components to increase effectiveness of PMTCT programmes, the consultation focused on the last two components of the strategy, as those are the main focus of the guidelines.
- b) Linking prevention and treatment is critical to increase uptake of essential prevention services and to ensure long-term care, treatment and support services. PMTCT programs should be implemented and scaled up as an important prevention intervention and an entry point to HIV-related care, treatment including HAART and

support for HIV-infected women, their children and families. HIV-care programmes should also include PMTCT as an important component.

- c) Pregnant women in need of HAART according to national and international guidelines should initiate treatment as soon as practicable. While the primary purpose is to improve and protect the health of the mother, the treatment is expected substantially to reduce MTCT risk;
- d) Situations requiring individualised patient management and special care are likely to arise in any programme or setting providing health care to pregnant women with HIV infection. However within the public health approach, programs built around a common regimen suitable for the majority of women are easier to implement and manage;
- e) Harmonisation of the PMTCT guidelines with the adult and paediatric treatment guidelines is necessary;
- f) Integrating PMTCT programs into existing health care services and creating new stand-alone programs has proven to be challenging, even if based around the simplest regimen (single-dose nevirapine for the mother and the infant). Once services permit, such programs should be encouraged to deliver HAART for pregnant women who have indications for initiating therapy for their own health or, for those who do not require therapy for their own health, provide the more efficacious, preferred PMTCT regimen based around short-course zidovudine plus single-dose nevirapine. In settings currently without the capacity to deliver the full range of antiretrovirals for PMTCT, it may still be feasible to implement the single-dose nevirapine regimen to ensure scale-up of PMTCT as a public health intervention. The expansion of PMTCT programs using single dose nevirapine still the best alternative whilst the necessary improvements in health systems are taking place to enable more complex antiretroviral regimens to be delivered.
- g) There remain concerns regarding possible emergence of nevirapine resistance associated with both single dose nevirapine as well as combination prenatal regimens using nevirapine and implications of such resistance on future treatment options for mothers or infants who become infected despite prophylaxis.

Participants at the Technical Consultation recommended the following regimens:

Maternal HAART available

- **Maternal HAART indicated** (table 1 column A). Women should start HAART at any time in pregnancy as appropriate and infants should receive zidovudine for 7 days from birth.
- **Maternal HAART considered** (table 1 column B): the revised WHO adult antiretrovirals guidelines recommend HAART to be considered for patients with clinical stage I and II with CD4 cell count below 350/mm³, particularly if closer to 200-250/mm³. Toxicity related to the initiation of long-term nevirapine-containing HAART may be a concern in pregnant women with CD4 count between 250 and 350/mm³. Recent data from resource-limited settings suggest a low toxicity associated with the use of nevirapine in this context. However this issue must continue to be carefully followed. The expert of the Technical Consultation concluded that nevirapine-containing HAART can be considered in this subgroup, or

alternatively a triple Non-Reverse-Transcriptase Inhibitor (NRTI) regimen. Infants should receive zidovudine for 7 days from birth.

- **Maternal HAART not indicated** (table 1 column C): Women should receive a short-course PMTCT regimen consisting of zidovudine starting at 28 weeks of pregnancy or as soon as feasible thereafter, continued in labour with single dose nevirapine at the onset of labour. Infants should receive a single dose of nevirapine within 72 hours of birth and zidovudine for 7 days from birth. If the woman receives at least 4 weeks of zidovudine before delivery, omission of the maternal nevirapine dose may be considered. A seven-day regimen of zidovudine/lamivudine given to the mother after delivery may be considered to reduce the emergence of nevirapine resistance.
- **In all cases (HAART indicated, considered or not indicated)**, if the mother receives less than 4 weeks of zidovudine or HAART before delivery, infant zidovudine dosing should be extended to a total of 4 weeks.

Maternal HAART not available

- **HAART is not available – Capacity to deliver the full range of antiretrovirals for PMTCT exists** (table 1 column C): all women and their infants should receive PMTCT antiretroviral regimens similar to those described when HAART is available and not yet indicated. If the woman is symptomatic, a seven-day regimen of zidovudine/ lamivudine given to the mother after delivery is advised when available to reduce the emergence of nevirapine resistance.
- **HAART is not available – Capacity to only deliver minimal range of antiretrovirals for PMTCT exists** (e.g. zidovudine not available) (table 1 column D): The minimal recommended regimen consists of single-dose nevirapine for the mother at onset of labour and single-dose nevirapine for the infant within 72 hours of birth .

Women first presenting around delivery and having received no antiretroviral for PMTCT

Women in labour when first accessing PMTCT interventions, who are known to be infected with HIV, and did not receive any antiretrovirals during this pregnancy should receive one of the following regimens:

- Where capacity to deliver the full range of antiretrovirals for PMTCT exists (option 1) single-dose nevirapine and zidovudine given to the mother during labour and single-dose nevirapine and four weeks of zidovudine from birth given to the infant, or (option 2) zidovudine/ lamivudine during delivery and for 7 days postpartum given to the mother and zidovudine/ lamivudine for 7 days given to the infant from birth.
- Where capacity to only deliver minimal range of antiretrovirals for PMTCT exists: single-dose nevirapine for the mother during labour and single-dose nevirapine for the infant within 72 hours of birth.

In case the mother received either single-dose nevirapine alone or in combination with zidovudine, a seven-day regimen of zidovudine/ lamivudine given to the mother after delivery can be considered when available to reduce the emergence of nevirapine resistance.

In case a woman did not receive any antiretrovirals during pregnancy and delivery, the infant should receive single-dose nevirapine within 72 hours of birth, plus 7 days of zidovudine if possible.

In all cases, such women need to be assessed postpartum for need for therapy.

Pregnant HIV-infected women with tuberculosis

In the rifampicin-containing phase of tuberculosis treatment, there are concerns about interaction when using nevirapine-containing HAART at the same time.

- If a pregnant woman has tuberculosis and HAART is initiated, consider:
 - Triple NRTI
 - EFV Efavirenz - based regimen. Efavirenz should be avoided in women of childbearing potential unless adequate contraception is available and used. If efavirenz has to be used, it should only be taken in the second and third trimesters of pregnancy. Adequate contraception must be made available postpartum, and the woman must be counselled about the importance of avoiding pregnancy if she would continue efavirenz therapy.

The issue of protease-inhibitor-containing regimens is being reviewed to be included in the revised adult treatment guidelines where appropriate guidance will be provided.

- If a pregnant woman is on HAART and develops tuberculosis, change to one of the above mentioned regimens.

As a general principle, if HAART is required, tuberculosis should be treated and the patient stabilized first. The full PMTCT regimen should be started and then HAART initiated as soon as possible

Considerations for breastfeeding women

Women with indications for antiretroviral treatment and who are breastfeeding should continue their antiretroviral regimen. The current United Nations recommendations on HIV and infant feeding remain unchanged for women receiving antiretroviral treatment, that is, HIV-infected women should avoid all breastfeeding when replacement feeding is acceptable, feasible, affordable, sustainable and safe. Otherwise, exclusive breastfeeding is recommended during the first months of life.

More research is needed for evaluating safety and efficacy of ARV prophylaxis on the risk of early and/or late postnatal transmission.

The recommendations are summarised in tables 1 and 2.

Doses will be included in the full report.