The European AIDS Clinical Society (EACS) is a not-for-profit group of European physicians, clinicians and researchers in the field of HIV/ AIDS.

It aims to bring together scientists from all over Europe to help exchange the latest medical and scientific knowledge regarding clinical aspects of HIV/ AIDS and its complications.

European AIDS Clinical Society

Guidelines

Clinical Management and Treatment of HIV Infected Adults in Europe

Index

Panel Members

Nathan Clumeck,
Chair, Brussels, *Belgium*

Nikos Dedes,
Athens, *Greece*

Anton Pozniak,
London, *United Kingdom*

François Raffi,
Nantes, *France*

and the EACS Executive Committee

Abbreviations used throughout this document

- ABC=abacavir
- ART=antiretroviral therapy
- ATV=atazanavir
- CVD=cardiovascular disease
- d4T=stavudine
- ddI=didanosine
- DRV=darunavir
- EFV=efavirenz
- ETR = etravirine
- FDC=Fixed Dose Combination
- HBV=hepatitis B virus
- HCV=hepatitis C virus
- HDL-c=HDL-cholesterol
- IDV=indinavir
- IHD=ischemic heart disease
- LDL-c=LDL-cholesterol
- LPV=lopinavir
- MVC maraviroc
- NFV=nelfinavir
- NNRTI=non-nucleoside reverse transcriptase inhibitors
- NRTI=nucleos(t)ide reverse transcriptase inhibitors
- NVP=nevirapine
- PI=protease inhibitors
- PI/r=protease inhibitors pharmacologically boosted with ritonavir
- RAL raltegravir
- RTV=ritonavir (if used as booster= /r)
- SQV=saquinavir
- TC=total cholesterol
- TDF=tenofovir
- TG=triglycerides
- TPV=tipranavir
- ZDV=zidovudine

Assessment of HIV Infected Patients at Initial and Subsequent Visits

INITIAL VISIT

- Complete medical history
- Physical examination, including height, weight, BMI, blood pressure, waist circumference
- Laboratory evaluation
  - Confirmation of HIV antibody positive
  - Plasma HIV RNA
  - Resistance testing (genotype) with determination of HIV subtype
  - CD4 absolute count + percentage (optional: CD8 and %)
  - Complete blood count, AST, ALT, Alk phosphatase, calcium, phosphate, glucose, creatinine, calculated creatinine clearance
  - Antibody tests for toxoplasma, CMV, Hepatitis A, B and C and syphilis
  - Fasting blood glucose and lipids including fasting total LDL & HDL cholesterol, and triglycerides (see metabolic guidelines)
  - Urine dipstick for protein and sugar
  - HLA B*5701 determination (if available)
  - R5 tropism (if available)
  - Cardiovascular risk assessment
- Sexually Transmitted Infection screen if appropriate
- Women: cervical pap smear
- Assessment of social and psychological condition: provide support and counselling if needed
- Consider HAV and HBV vaccination (depending on serology results) and pneumococcal vaccination
- PPD if CD4 above 400. Negative PPD does not exclude active or latent tuberculosis. T.SPOT.TB® (or QuantiFERON-TB Gold IT®) can be an alternative to PPD in selected high risk populations (if available)

SUBSEQUENT VISITS

(Asymptomatic patients not receiving antiretroviral therapy)

- At least every 6 months
  - Complete blood count, CD4 count and %
  - Plasma HIV RNA
- Every year
  - Physical examination
  - Evaluation of social and psychological support,
  - Smoking cessation, diet evaluation

- Repeat serologic testing (syphilis, CMV, toxoplasmosis, hepatitis B, hepatitis C) if previously negative
- AST, ALT
- Women: cervical pap smear
- Fasting lipids

- Every 6 months
  - If cirrhosis (regardless of cause): alphafoetoprotein + ultrasound examination
- Treatment initiation
  - Assess and support patients' readiness to start combined ART (see specific Table)
  - Physical examination, including height, weight, BMI, blood pressure, waist circumference
  - Plasma HIV RNA
  - Resistance testing (genotype), if not yet obtained
  - CD4 count and % (optional: CD8 count and %)
  - Complete blood count, AST, ALT, bilirubin, creatinine, calculated creatinine clearance, calcium, phosphate
  - Fasting glucose and lipids
  - Urine dipstick for protein and sugar
  - Other laboratory parameters may be useful according to selected first-line regimen e.g. protein creatinine ratio, amylase, lipase
  - Cardiovascular risk assessment
- Visits on therapy
  - Plasma HIV RNA
  - CD4 count and % (optional: CD8 count and %)
  - Complete blood count, creatinine, calculated creatinine clearance, AST, ALT bilirubin
  - Other laboratory parameters according to selected regimen
  - Fasting glucose and lipids

"Assessing and supporting patients' readiness to start ART"[1]

Goal: Facilitate decision making and starting ART for patients who qualify according to international guidelines.

Before initiating ART, screen for decision making and adherence barriers:	
Patient related factors: A) Depression [2] B) Harmful alcohol or recreational drug use [3] C) Cognitive problems [4] D) Low health literacy.	**System related factors:** E) Health insurance and drug supply F) Continuity of drug supply G) Social support and disclosure.
Recognise, discuss and reduce problems wherever possible!	

Assess patients' readiness and support progress between stages [5]:
"I would like to talk about HIV-medication" <wait> "what do you think about it?" [6]

Remember:

- Set the agenda before every interview
- use open questions whenever possible
- use the WEMS-technique [7]

Precontemplation:
"I don't need it, I feel good"
"I don't want to think about it"

Support: Show respect for patient attitude / Try to understand health and therapy beliefs / Establish trust / Provide individualised short information / Schedule the next appointment.

Restage again

Contemplation: "I am weighing things up and feel torn about what to do about it"

Support: Allow ambivalence / Support to weigh pros and cons together with patient / Assess information needs and support information seeking / Schedule the next appointment.

NO

Restage again

Preparation "I want to start, I think the drugs will allow me to live a normal life"

Support: Reinforce decision / Make shared decision on most convenient regimen / Educate: adherence, resistance, side effects / Discuss integration into daily life / Assess self-efficacy

Ask: Do you think you can manage to take cART consistently once you have started?

Use: VAS 0-10 [8]

0 ----------5 ---------- 10

NO

Patients presenting in the clinic may be at different stages of readiness: Precontemplation, contemplation or preparation [Transtheoretic model; Prochaska JO. Am Psychol 47:1102-1114, 1992]. The first step is to assess this stage, and then to support/intervene accordingly. An exception is if a patient presents late or very late, i.e. <200 or <50 CD4/µl. In this case the initiation of ART should not be delayed; the clinician should try to identify the most important adherence barriers which may be present, and support the patient to be prepared for prompt initiation of ART."

Consider skills training:

- Medication-taking training, possibly MEMS (2-4wk) [9]
- Directly Observed Therapy with educational support
- Use aids: Pill boxes, cell phone alarm, involve contact persons where appropriate

START AND MAINTAIN ADHERENCE

Screen: For adherence problems in each meeting [10]

Support: Discuss side effects, educate about surrogate markers, discuss integration of drug taking schedule

Empower: Give positive feedback

EACS Guidelines ▪ Version 5

Clinical Management and Treatment of HIV Infected Adults in Europe

Comments to the table Start of ART and patients' readiness (1)

1 This table should facilitate the initiation of ART. Matters for consideration listed in this table, such as decision making or barriers to adherence, have to be judged clinically in their context. For instance the clinician has to judge whether ART has to be initiated immediately despite the detection of possible barriers to adherence or whether delaying initiation is justified. Consider patient's cultural background.

2 Ask: "During the past month have you often been bothered by feeling down, depressed or hopeless?" "During the past month have you often been bothered by little interest or pleasure in doing things?" "Is this something with which you would like help?" If answers are positive, then sensitivity is 96%, specificity 89% (Arroll B et al. BMJ 327:1144-1146. 2003).

3 Ask: "Have you thought about **C**utting down?" "Have you ever become **A**nnoyed when people talk to you about your drinking?" "Have you ever felt **G**uilty about your drinking?" "Do you ever have a drink first thing in the morning (**E**ye opener)?" An affirmative answer to more than two CAGE-questions means a sensitivity and specificity for problematic alcohol use of more than 90% (Kitchens JM. JAMA 272(22): 1782-1787. 1994.). Ask similar questions for recreational drug use.

4 Ask: "Do you feel that you are having problems concentrating in your daily life?" "Do you feel slow in your thinking?" "Do you feel that you are having problems with your memory?" "Have relatives or friends expressed that they feel you are having problems with your memory or difficulty concentrating?"

5 Patients presenting in the clinic may be at different stages of readiness: Precontemplation, contemplation or preparation [Transtheoretic model; Prochaska JO. Am Psychol 47:1102- 1114, 1992]. The first step is to assess this stage, and then to support/intervene accordingly. An exception is if a patient presents late or very late, i.e. <200 or <50 CD4/µl. In this case the initiation of ART should not be delayed; the clinician should try to identify the most important adherence barriers which may be present, and support the patient to be prepared for prompt initiation of ART.

6 This is a suggested opening question to assess the patient's stage of readiness. Further discussion will indicate which of the three initial stages the patient has reached: he/she might even be ready for therapy.

7 WEMS: Waiting (>3sec), Echoing, Mirroring, Summarising (Langewitz W et al. BMJ 325:682-683. 2002).

8 VAS (= Visual Analogue Scale; Range from 0 to 10 i.e. 0 = I will not manage, 10 = I am sure I will manage).

9 Medication training/ MEMS training could be done with vitamins before starting ART.

10 Suggested adherence questions: "In the past 4 wks how often have you missed a dose of your HIV medication: every day, more than once a wk, once a wk, once every 2 wks, once a month, never?" "Have you missed more than one dose in a row?" (Glass TR et al. Antiviral Therapy 13(1):77-85. 2008).

Adapted from: J. Fehr, D. Nicca, F. Raffi, R. Spirig, W. Langewitz, D. Haerry, M.Battegay, NEAT, 2008.

Primary HIV infection (PHI)

Definition of Acute primary HIV infection

- High risk exposure within previous 2-8 weeks,
- and Clinical symptoms,
- and detectable HIV in the plasma (p24 Ag and/or HIV RNA > 10 000 c/ml)
- and negative or indeterminate serologic testing (negative or weakly positive ELISA, and WB ≤1 band)
- Recommendation: confirm HIV infection by HIV antibody test (WB) performed 3-6 weeks later.

Treatment:

- Treatment indicated if:
  - AIDS defining events
  - Confirmed CD4 <350/mm3 at month 3 or beyond
- Treatment should be considered if:
  - Severe illness/ prolonged symptoms (especially CNS symptoms)
- If treatment of PHI is considered, patient should be recruited into ongoing clinical trial
- Treatment optional, as indication relies only on theoretical considerations. In most situations, wait till month 6 (with CD4 and plasma HIV-RNA monitoring) and follow criteria for initiation of treatment in chronic HIV infection. Some experts recommend treatment as a tool for prevention of HIV transmission.
  Duration of treatment: unknown but maybe should be lifelong.
  Maintain closer follow-up in case of treatment interruption

Resistance testing:

- Recommended in all situations as soon as acute HIV infection is diagnosed, even if treatment not initiated
- In case it cannot be performed, store blood for further testing.

Transmission:

- Recognize sexually transmitted infections (STIs), including syphilis, gonorrhoea, Chlamydia (Urethritis and LGV), HPV, hepatitis B and hepatitis C.
- Counsel newly diagnosed patient on high risk of transmission and preventive measures (condoms) including notifying and testing partners.

Recommendations for Initiation of Therapy in Naive HIV-Infected Patients

SYMPTOMATIC	• CDC stage B and C: treatment recommended • If OI, initiate as soon as possible*
ASYMPTOMATIC	• CD4 < 200: Treatment recommended, without delay. • CD4 201-350: treatment recommended. • CD4 350-500: - Treatment recommended if hepatitis C co-infection, hepatitis B co-infection requiring therapy, HIV-associated nephropathy or other specific organ deficiency; - Treatment should be considered if VL>10^5 c/ml and/or CD4 decline >50-100/mm^3/year or age >50 or, pregnancy, high cardiovascular risk, malignancy. • CD4 > 500: - Treatment should generally be deferred, independently of plasma HIV RNA; closer follow-up of CD4 if VL > 10^5 c/ml. - Treatment can be offered if presence of ≥ 1 of the above co-morbid conditions (CD4 350-500). • Whatever CD4 and Plasma HIV RNA, treatment can be offered on an individual basis, especially if patient is seeking and ready for ARV therapy
RESISTANCE TESTING	Genotypic testing and subtype determination recommended, ideally at the time of HIV diagnosis, otherwise before initiation of first-line regimen If genotypic testing is not available, a ritonavir-boosted PI should be included in the first-line regimen
ADDITIONAL REMARKS	• Before starting treatment, CD4 should be repeated and confirmed • Time should be taken to prepare the patient, in order to optimize compliance and adherence**

* Pay particular attention to drug-drug interactions, drug toxicities, immune reconstitution syndrome and adherence, etc…

** See recommendation on "Assessing and supporting patients' readiness to start ART"

Initial Combination Regimen for Antiretroviral-Naïve patient

SELECT 1 DRUG IN COLUMN A AND 1 NRTI COMBINATION IN COLUMN B	A	B	REMARKS
Recommended	NNRTI • EFV[1] • NVP[5] or ritonavir-boosted PI • ATV/r[6] • DRV/r[6] • LPV/r[7] • SQV/r	TDF/FTC ABC/3TC[2-3-4]	- TDF/FTC co-formulated - ABC/3TC co-formulated - EFV/TDF/FTC co-formulated - ATV/r: 300/100 mg qd - DRV/r: 800/100 mg qd - LPV/r:400/100 mg bid or 800/200 mg qd - SQV/r:1000/100 mg bid
Alternative	SQV/r FPV/r RAL[9]	• ZDV/3TC[8] • ddI/3TC or FTC[8]	- SQV/r: 2000/100 mg qd - FPV/r:700/100 mg bid or 1400/200 mg qd - RAL: 400 mg bid - ZDV/3TC co-formulated

1 EFV: not recommended in pregnant women or women with no reliable and consistent contraception; not active on HIV-2 and HIV-1 group O
2 Contra-indicated if HLA B*5701 positive. Even if HLA B*5701 negative, counselling on HSR risk still mandatory
3 ABC + NVP contra-indicated, unless HLA B*5701 negative
4 Abacavir should be used with caution in patients with a high cardiovascular risk and/or patients with a viral load higher than 100,000 copies/ml.
5 NVP: Use with extreme caution in women with CD4 >250 and men with CD4 >400/µL; not active on HIV-2 and HIV-1 group O
6 Castle study (LPV/r vs ATV/r) has shown better tolerability of ATV/r and Artemis study (LPV/r vs DRV/r) better efficacy and greater tolerability of DRV/r.
7 ACTG 5142, randomised study showed lower virological efficacy of LPV/r vs EFV. However no PI mutations were seen in the LPV/r failures.
8 Only if unavailable or intolerant to other recommended NRTIs
9 Raltegravir is indicated in combination with other anti-retroviral medicinal products for the treatment HIV-1 infection in adult patients. It has been studied only in combination with TDF/FTC in naïve patients with limited follow-up (48 weeks).

HAART in TB/HIV co-infection

Suggested timing of HAART initiation in TB/HIV coinfection according to CD4/μl

CD4 COUNT, CELLS/μl	WHEN TO START HAART
<100	As soon as practical
100–350	As soon as practical, but can wait until after completing 2 months TB treatment especially when there are difficulties with drug interactions, adherence and toxicities
>350	At physician discretion

Concomitant use of anti-TB medications and antiretrovirals

- NRTIs: no significant interaction with rifampicin nor rifabutin
- NNRTIs:
  - EFV and rifampicin: EFV 800mg qd if weight >60kg, 600 mg qd if <60kg; rifampicin at standard dose. Some physicians prefer not to dose adapt efavirenz as data are controversial. In any case TDM is recommended after 2 weeks.
  - EFV and rifabutin: EFV at standard dose; rifabutin 450mg daily
  - NVP: not recommended
  - Etravirine: not recommended
- PIs
  - and rifampicin: not recommended
  - and rifabutin: rifabutin 150 mg x 3 per week with ATV/r, DRV/r, LPV/r or SQV/r; PI/r at standard dose; monitor liver enzyme tests and, whenever possible, perform TDM for PI
- Raltegravir
  - and rifampicin: use with caution (only if no alternative), if used: raltegravir 800 mg bid
  - and rifabutin: no data
- Maraviroc
  - and rifampicin: use with caution at double dose 600mg bd maraviroc
  - and rifabutin: standard doses
- Enfuvirtide: no significant interaction with rifampicin nor rifabutin

Where combinations are not recommended, specialist HIV treatment advice should be sought. TDM of NNRTI and PI should be performed when drug regimens contain one of these drugs. Drug levels of anti-tuberculosis drugs should be measured when there is clinical concern regarding absorption or response to TB therapy.

Recommended 1st line ARV combination in patients receiving anti-TB medication

Among recommended regimens for antiretroviral-naïve patients, preference should be given to EFV/TDF/FTC with dose adaptation of EFV if needed (cf above).
Alternative =

- recommended PI/r + TDF/FTC, using rifabutin instead of rifampicin;
- Use with caution
  1. raltegravir 800 mg bid + TDF/FTC with rifampicin
  2. if plasma viral load < 100,000 c/ml, fixed-dose combination of ZDV/ABC/3TC bid +/- tenofovir, could also represent a short term alternative until TB treatment has been completed.

If it is not possible to use these drugs because of resistance/intolerance seek expert help.

Switch strategies for virologically suppressed patients (confirmed plasma viral load < 50 c/ml)

Indication:
- Documented toxicity
- Side-effects
- Planned pregnancy
- Wish to simplify regimen
- Actual regimen no longer recommended
- Prevention of long-term toxicity (pre-emptive switch)
- Aging and/or co-morbidity with a possible negative impact of drug(s) in current regimen eg on CVS risk, metabolic parameters.
- Management of potential drug interactions
- Management of TB, HBV or HCV infection

Principles:
1. Intra-class switch if drug-specific related adverse event
2. Bid to qd NRTI switch for simplification, prevention of long-term toxicity
3. PI/r to NNRTI switch for simplification, prevention or improvement of metabolic abnormalities, adherence facilitation. NVP has the advantage of its metabolic profile. EFV has the advantage of possible FDC of 3 drugs (Atripla®).
4. Switching from PI/r to NNRTI or raltegravir only possible if 1) no history of prior virological failure; and 2) NRTI backbone fully active.
5. PI/r or enfuvirtide to raltegravir switch for simplification, prevention or improvement of metabolic abnormalities, adherence facilitation.
6. Simplification of a complex multi-drug regimen in antiretroviral-experienced patients with 1) substitution of drugs difficult to administer (enfuvirtide) and/or with poor activity (NRTI in case of multiple NRTI resistance) and/or poor tolerability and 2) addition of new well-tolerable, simpler and active agent(s).

Strategies not recommended:
a. Intermittent therapy, sequential or prolonged treatment interruptions
b. 2 drug combination,i.e. 1 NRTI + 1 NNRTI or 1 NRTI + 1 PI without ritonavir or 1 NRTI + RAL, or 2 NRTIs
c. NRTI-sparing regimen except if documented intolerance to all NRTIs
d. Triple NRTIs combinations

Other strategy:

PI/r monotherapy with bid LPV/r ,or qd DRV/r, might represent an option in patients with intolerance to NRTI or for treatment simplification. Such strategy only applies to patients without history of failure on prior PI-based therapy and who have had viral load < 50 c/ml in at least the past 6 months.

Virological Failure

Definition	Confirmed plasma HIV RNA > 50 copies/ml 6 months after starting therapy (initiation or modification) in patients that remain on ART
General measures	• Evaluate adherence, compliance, tolerability, drug-drug interactions, drug-food interactions, psychosocial issues • Perform resistance testing on failing therapy (usually reliable with plasma HIV RNA levels >500-1000 copies/ml) and obtain historical resistance testing for archived mutations • Consider TDM • Review antiretroviral history • Identify treatment options, active, potentially active drugs/combinations
Management of virological failure (VF)	If plasma HIV RNA > 50 and <500-1000 copies/ml • Check for adherence • Check plasma HIV RNA 1 to 2 months later • Improve boosted PI's PK (if applicable) If plasma HIV RNA confirmed > 500/1000 copies/ml, change regimen as soon as possible: what to change will depend on the resistance testing results: • No resistance mutations found: re-check for adherence, perform TDM • Resistance mutations found: switch to a suppressive regimen based on drug history; multidisciplinary experts discussion advised Goal of new regimen: plasma HIV RNA < 400 c/ml after 3 months, plasma HIV RNA < 50 c/ml after 6 months
In case of resistance mutations demonstrated	<u>General recommendations:</u> • Use 2 or preferably 3 active drugs in the new regimen (including active drugs from previously used classes) • Any regimen should use at least1 fully active PI/r (e.g. darunavir/r) plus 1 drug from a class not used previously e.g. fusion, integrase or CCR inhibitor (if tropism test shows R5 virus only), or 1 NNRTI (e.g. etravirine), assessed by genotypic testing • Defer change if < 2 active drugs available, based on resistance data, except in patients with low CD4 count (<100/mm3) or with high risk of clinical deterioration for whom the goal is the preservation of immune function through partial reduction of Plasma HIV RNA (> 1 log reduction) by recycling. • If limited options, consider experimental and new mechanistic drugs, favouring clinical trials (but avoid functional monotherapy) • Treatment interruption is not recommended <u>Optimisation of new regimen:</u> • If demonstrated NRTI multiple resistance, avoid NRTI but • Consider continuation of 3TC or FTC even if documented resistance mutation (M184V/I) • Select 1 active ritonavir-boosted PI. If at all possible avoid double boosted PIs • Etravirine potentially active in selected NNRTI-mutation profiles • Always check for drug-drug-interactions, and when necessary perform TDM of drugs of new regimen if available If many options are available, criteria of preferred choice include: simplicity of the regimen, toxicity risks evaluation, drug-drug-interactions, future salvage therapy

EACS Guidelines ▪ Version 5

Clinical Management and Treatment of HIV Infected Adults in Europe

Treatment of HIV Pregnant Women

Pregnant women should be monitored every month and as close as possible to the predicted delivery date.

Criteria for starting ART in pregnant women (see different scenarios)	Same as for non pregnant
Objective of treatment in pregnant women	Full Plasma HIV RNA suppression by third trimester and specifically at time of delivery
Resistance testing	Same as for non pregnant, i.e. before starting ART and in case of virological failure
SCENARIO 1 Women becoming pregnant while already on ART 2 Women becoming pregnant while treatment naïve and who fulfil the criteria (CD4) for initiation of ART 3 Women becoming pregnant while treatment naïve and who do not fulfil the criteria (CD4) for initiation of ART 4 Women whose follow up starts after W28 of pregnancy	 1 Maintain ART but switch drugs that are potentially teratogenic 2 Start ART at start of 2nd trimester is optimal 3 Start ART at start of W28 of pregnancy (at the latest 12 weeks before delivery); start earlier if high plasma viral load or risk of prematurity 4 Start ART immediately
Antiretroviral regimen in pregnancy	Same as non pregnant, • except avoid EFV • NVP not to be initiated but continuation is possible if started before pregnancy • Among PI/r, prefer LPV/r or SQV/r or ATV/r • RAL, DRV/r: few data available in pregnant women • ZDV should be part of the regimen if possible
Drugs contra-indicated during pregnancy	Efavirenz, ddI + d4T,Triple NRTI combinations
IV zidovudine during labour	Benefit uncertain if Plasma HIV RNA < 50 c/ml
Single dose nevirapine during labour	Not recommended
Caesarean section	Benefit uncertain if Plasma HIV RNA < 50 c/ml at W34-36

EACS Guidelines ▪ Version 5

Clinical Management and Treatment of HIV Infected Adults in Europe

Post-Exposure Prophylaxis

	POST-EXPOSURE PROPHYLAXIS (PEP) RECOMMENDED IF	
	Nature of exposure	**Status of source patient**
Blood	Subcutaneous or intramuscular penetration with IV or IM needle, or intravascular device	HIV + Or serostatus unknown but presence of HIV risk factors
	• Percutaneous injury with sharp instrument (lancet), IM or SC needle, suture needle • Contact > 15 min of mucous membrane or non intact skin	HIV +
Genital secretions	Anal or vaginal sex	HIV + Or serostatus unknown but presence of HIV risk factors
	Receptive oral sex with ejaculation	HIV +
Intravenous drug user	Exchange of syringe, needle, preparation material or any other material	HIV +

- Rapid testing of the source patient for HCV and HIV (if HIV status unknown) recommended,
- If source patient HIV+ on ARV therapy, order genotyping testing if HIVRNA > 1000 copies/µL
- If prior resistance test available in source patient, individualize the PEP therapy accordingly
- PEP to be started ideally < 4 hours after the exposure, and no later than 48 hours
- Duration of PEP: 4 weeks
- Standard PEP regimen: TDF/FTC (alternative: ZDV/3TC) + LPV/r tablets 400/100 mg bid
- Full sexual health screen in case of sexual exposure
- Follow-up:
  - HIV serology + HBV and HCV, pregnancy test
  - (women) within 48 hours of exposure
  - Reevaluation of PEP indication by HIV expert within 48-72 hours
  - Assess tolerability of ARV PEP regimen
  - Transaminases, HCV-PCR and HCV serology at month 1 if source of exposure were HCV+ (observed or suspected)
  - Repeat HIV serology after 2 and 4 months, syphilis serology after 1 month if sexual exposure