THE STAGING AND MEDICATION OF HIV INFECTION

Supplement A: WHO CLINICAL STAGING

Clinical Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage 2

- Moderate unexplained weight loss (under 10% of presumed or measured body weight)
- Recurrent respiratory tract infections (sinusitis, tonsilitis, otitis media, pharyngitis)
- Herpes zoster
- Angular chelitis
- Recurrent oral ulcerations
- Papular pruritic eruptions
- Seborrheic dermatitis
- Fungal nail infections

Clinical Stage 3

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhea for longer than one month
- Unexplained persistent fever (above 37.6°C, intermittent or constant, for longer than one month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (current)
- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteremia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anemia (<8 g/dl), neutropenia ($<0.5 \times 10^9$ per liter)
- Chronic thrombocytopenia ($<50 \times 10^9$ per liter)

Clinical Stage 4

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Esophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis (with diarrhea)
- Chronic isosporiasis
- Disseminated mycosis (coccidiomycosis or histoplasmosis)
- Recurrent non-typhoidal salmonella bacteremia
- Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumors
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

Supplement B: Basic considerations regarding ARV medication and pregnancy

Antiretroviral agent	Maternal antiretroviral intervention during pregnancy, labor, delivery and thereafter			Infant prophylaxis Infant concerns
	Maternal concerns	Placental Passage	Infant concerns	
Nucleoside reverse transcriptase inhibitors				
Abacavir (ABC)	Risk of hypersensitivity reactions (5–8% of non-pregnant women; rate in pregnancy unknown)	Yes	Limited data available: animal studies suggest potential skeletal malformations with in utero exposure to drug levels 35 times that of human exposure	Not recommended
Emtricitabine (FTC)	No specific concerns	Yes	No specific concerns	Not recommended
Lamivudine (3TC)	Favorable safety profile: concern of hepatitis B flare if mother is HBV-coinfected and drug is stopped	Yes	Favorable safety profile	Limited safety data available
Tenofovir (TDV)	Risk of renal toxicity warrants monitoring; concern of hepatitis B flare if mother HBV co-infected and agent stopped postpartum	Yes	Concern of fetal bone defects; potential concern of low birth	Not recommended
Zidovudine (AZT)	Well tolerated; risk of anemia	Yes	Favorable safety profile	Favorable safety profile, may be associated with anemia that is reversible when stopped
Non-nucleoside reverse transcriptase inhibitors				
Efavirenz (EFV)	Associated with rash, neuropsychiatric disturbances	Yes	Potential risk	Not recommended
Nevirapine (NVP)	Potential risk of hypersensitivity reactions including rash and hepatic toxicity; incidence in women with CD4 between 250 and 250 cells/mm^3 unknown but strong consensus that benefit exceeds risk in women requiring ART; not recommended in women with CD4 >350 cells/mm^3 because of higher toxicity risk	Yes	Favorable safety profile	Favorable safety profile, including during extended dosing (documented until 6 months) in infants receiving breast milk
Protease inhibitors				
Lipinavir/ritonavir (LPR/r)	Well tolerated: concern of hyperlipidemia, insulin resistance, hyperglycemia, and rarely diabetes mellitus	Yes (but low approximately 20%)	Concern of preterm delivery	Not recommended

Supplement C: ARV medications and associated toxicities

ARV drug	Common associated toxicity	Suggested substitute
Nucleotide reverse transcriptase inhibitors (NtRTIs)		
TDF **Tenofovir** **Viread**	Asthenia, headache, diarrhea, nausea, vomiting, flatulence Renal insufficiency, Fanconi syndrome Osteomalacia Decrease in bone mineral density Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue TDV	If used in first-line therapy, AZT (or d4T if no other choice) If used in second-line therapy, there is no option if patient has failed AZT/d4T in first line therapy. If feasible, consider referral to a higher level of care where individualized therapy may be available
Nucleoside reverse transcriptase inhibitors (NRTIs)		
D4T **Stavudine** **Zerit**	Pancreatitis Peripheral neuropathy Rapidly progressive ascending neuromuscular weakness (rare) Lactic acidosis, severe hepatomegaly with steatosis	No longer recommended for use because of toxicities – only consider if there are no other options
ABC **Abacavir** **Ziagen**	Severe hypersensitivity reaction (can be fatal) Lactic acidosis, severe hepatomegaly with steatosis Nausea, vomiting	
AZT **ZDV** **Zidovudine** **Retrovir**	Bone marrow suppression, macrocytic anemia or neutropenia Gastrointestinal intolerance, headache, insomnia, asthenia Skin and nail pigmentation Lactic acidosis with hepatic steatosis	If used in first line therapy, TDF (or d4T if no other choice) If used in second line therapy, d4T
3TC **Lamivudine** **Epivir**	Abdominal pain, nausea, diarrhea, rash and pancreatitis	
ddI **Didanosine** **Videx**	Pancreatitis, lactic acidosis, neuropathy, diarrhea, abdominal pain, nausea	
FTC **Emtricitabine** **Emtriva**	Headache, nausea, vomiting, diarrhea, rash Skin discoloration (mild hyperpigmentation on palms and soles)	
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)		
EFV **Efavirenz** **Sustiva**	Hypersensitivity reaction Stevens-Johnson syndrome Rash Hepatic toxicity, transaminase elevation False-positive cannabinoid test Persistent and severe CNS toxicity (dizziness, impaired concentration, insomnia, abnormal dreams, depression, confusion) Hyperlipidemia Male gynecomastia Potential teratogenicity (first trimester of pregnancy or women not using contraception)	NVP bPI if intolerant to both NNRTIs Triple NRTI if no other choice **Medications which should be avoided: antifungal (voriconazole), midazolam, triazolam, ergot derivatives, cisapride, St John's wort

Supplement C: ARV medications and associated toxicities

ARV drug	Common associated toxicity	Suggested substitute
NVP	Hypersensitivity reaction Stevens-Johnson syndrome Rash Hepatic toxicity Hyperlipidemia	EFV bPI if intolerant to both NNRTIs Triple NRTI if no other choice
Protease inhibitors (PIs)		
Potential drug interactions (drugs to be avoided): **Antimycobacterials:** *Rifampin*: decreases plasma concentration of PIs by approximately 90% **Benzodiazepines:** *midazolam, triazolam*: potential for prolonged or increased sedation or respiratory depression **Ergot derivatives:** *Dihydroergotamine, ergotamine, ergonovine, methylergonovine*: potential acute ergot toxicity characterized by peripheral vasospasm and ischemia of extremities and other tissues **GI motility agents:** *cisapride*: potential cardiac arrhythmias **HMG-CoA reductase inhibitors:** *lovastatis, simvastatin*: potential myopathy, including rhabdomyolysis **Neuroleptic:** *pimozide*: potential cardiac arrhythmia **St John's wort:** decreased plasma concentration of PI		
ATV/r **Atazanavir/ritonavir**	Indirect hyperbilirubinemia Clinical jaundice Prolonged PR interval – first degree symptomatic AV block in some patients Hyperglycemia Fat misdistribution Possible increased bleeding episodes in individuals with hemophilia Nephrolithiasis	LPV/r
LPV/r **Liponavir/ritonavir** **Kaletra**	GI intolerance, nausea, vomiting, diarrhea Asthenia Hyperlipidemia (especially hypertriglyceridemia) Elevated serum transaminases Hyperglycemia Fat misdistribution Possible increased bleeding episodes in patients with hemophilia PR interval prolongation QT interval prolongation and torsades de pointes	ATV/r
RTV **Ritonavir** **Norvir**	Weakness, diarrhea, nausea Circumoral paresthesia Taste alteration Elevated cholesterol and triglycerides	
SQV **Saquinavir** **Invirase**	Diarrhea, abdominal pain, nausea Hyperglycemia Elevated LFTs Should not be taken with garlic supplements (drug level could be lowered)	
Fusion Inhibitor		
T-20 **Enfuviritide** **Fuzeon**	Local injection site reactions, Bacterial pneumonia Insomnia, depression Peripheral neuropathy Cough	

Supplement D: ARV DRUG DOSING

Generic Name	Dose
NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)	
Abacavir (ABC)	300 mg twice daily 600 mg once daily
Didanosine (ddl)	400 mg once daily (>60 kg) 250 mg once daily (<60 kg)
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily 300 mg once daily
Zidovudine (AZT)	250 to 300 mg twice daily
NUCLEOTIDE REVERSE TRANSCRIPTACE INHIBITORS (NtRTIs)	
Tenofovir (TDF)	300 mg once daily Adjustment required for those with altered creatinine clearance can be considered using the Cockcroft-Gault formula
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS	
Efavirenz (EFV)	600 mg once daily
Etravirine (ETV)	200 mg twice daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily
PROTEASE INHIBITORS	
Atazanavir + ritonavir (ATV/r)	300 mg + 100 mg once daily
Darunavir + ritonavir (DRV/r)	600 mg + 100 mg twice daily
Fos-amprenavir + ritonavir (FPV/r)	700 mg + 100 mg twice daily
Indinavir + ritonavir (IDV/r)	800 mg + 100 mg twice daily
Lopinavir/ritonavir (LPV/r)	Fixed dose combination tablets (LPV 200 mg/RTV 50 mg) Two tablets (400 mg/100 mg) twice daily
	Considerations for individual on TB therapy In the presence of rifabutin, no dose adjustment required In the presence of rifampin, use ritonavir super boosting (LPV 400 mg + RTV 400 mg twice daily) or LPV 800 mg + RTV 200 mg twice daily with close clinical and hepatic enzyme monitoring
Saquinavir + ritonavir (SQV/r)	1000 mg + 100 mg twice daily
	Considerations for individuals on TB therapy In the presence of rifabutin, no dose adjustment required In the presence of rifampicin, use ritonavir super boosting (SQRV 400 mg + RTV 400 mg twice daily) with close clinical and hepatic enzyme monitoring
INTEGRASE STRAND TRANSFER INHIBITORS (INSTIs)	
Raitegravir (RAL)	400 mg twice daily

PREVENTION:
MATERNAL TO CHILD TRANSMISION (MCT)

Clinical scenario	Suggested regimen
Pregnant women tested HIV-infected and eligible for ART	AZT + 3TC + NVP or TDF + 3TC (or FTC) + NVP or AZT + 3TC + EFV or TDF + 3TC (or FTC) or EFV
Pregnant women eligible for ART but exposed to sd-NVP without dual NRTI tail in last 12 months	Non-NNRTI regimen
Pregnant women eligible for ART who have clinically significant or documented severe anemia (Hemaglobin <7 g/dl)	TDF + 3TC (or FTC) + EFV or TDF + 3TC (or FTC) + NVP
Pregnant women eligible for ART with HIV-2 infection alone	AZT + 3TC + ABC or AZT + 3TC + LPV/r
Pregnant women eligible for ART with TB coinfection	AZT + 3TC + EFV TDF + 3TC (or FTC) + EFV
Pregnant women eligible for ART with HBV coinfection reporting HBV treatment	TDF + 3TC (or FTC) + EFV or TDF + 3TC (or FTC) + NVP
Non-pregnant women of childbearing age who are eligible for ART and who may become/plan to become pregnant	AZT + 3TC + NVP or TDF + 3TC (or FTC) + NVP
Women receiving ART who become pregnant	Continue same ART

A note on abbreviations

ARV (antiretrovirals) – treatments that inhibit growth and/ or transmission of retroviral infections
ART (antiretroviral therapy) – treatment with anti-retroviral medications
HAART (highly active antiretroviral therapy) – treatment with combinations of potent antiretroviral medications (typical 3 or more different medications)

This Supplement is designed to be read in association with the Wall Chart entitled "*The Prevention of HIV Transmission*". It has been prepared by and developed by:

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