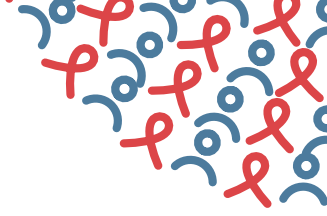




ADVANCED HIV DISEASE MANAGEMENT AND CARE

HANOI, SEPTEMBER 2021





Introduction

“ This job aide was designed to assist health staff working at out-patient HIV treatment facilities in Vietnam. It includes relevant definitions and client flow algorithms to support screening for, and treatment of common opportunistic infections in patients with advanced HIV disease (AHD), and provides guidance for preventive treatment.

The content in this document is based on Ministry of Health's Decision no. 5456/QĐ-BYT on National guidelines on HIV/AIDS Treatment and care dated 20/11/2019, Decision No. 4067/QĐ-BYT on National guidelines on tuberculosis active case finding and latent tuberculosis treatment dated 24/8/2021.

The document is organized as follows:

1 Definition of AHD

2 Diagnosis and prophylaxis package of care for individuals with AHD

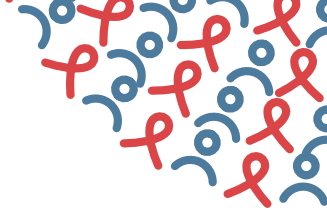
- Overview of services for persons with AHD
 - Table of components for diagnosis and prophylaxis package of care
 - TB screening and latent TB treatment
 - Co-trimoxazol prophylaxis
 - Prophylaxis for cryptococcosis
-

3 Screening for and management of common opportunistic infections in patients with AHD

- Respiratory symptoms
- Nerve symptoms
- Diarrheal symptoms
- Skin lesions
- Swallowing pains



For the most updated version, please visit: <https://hub.skconnect.org/documentation/quan-ly-va-cham-soc-benh-hiv-tien-trien/tation/quan-ly-va-cham-soc-benh-hiv-tien-trien/>



Abbreviation

1HP	1-month isoniazid and rifapentine regimen, daily
3HP	3-month isoniazid and rifapentine regimen, once a week
3HR	3-month isoniazid and rifampicin regimen, daily
4R	4-month rifampicin regimen, daily
6H	6-month isoniazid regimen, daily
6L	6-month levofloxacin regimen, daily
AHD	Advanced HIV disease
ART	antiretroviral therapy
ARV	Antiretroviral
CNS	Central neuros system
CMV	Cytomegalovirus
CrAg	Cryptococcal antigen
DTG	Dolutegravir
EFV	Efavirenz
INH (H)	Isoniazid
CRP	C - reactive protein
HIV	Human Immunodeficiency Virus
MTB/RIF	Mycobacterium Tuberculosis/Rifampicin
LF-LAM	Lateral flow lipoarabinomannan assay
NVP	Nevirapine
RAL	Raltegravir
RIF (R)	Rifampicin
OI	Opportunistic infection
P	Rifapentine
PIs	Proteases
PCP	Pneumocystis jiroveci Pneumonia
TB	Tuberculosis
TDF	Tenofovir
TMP - SMX	Trimethoprim - Sulfamethoxazole
WHO	World Health Organization



1 Definition of advanced HIV disease (AHD)

Adults, adolescents and children ≥ 5 years of age with CD4 count < 200 cells/mm³ or at WHO clinical stage 3 or 4.

All children < 5 years of age with HIV infection are considered to have advanced HIV disease.

It is necessary to assess clinical staging at all visits and to conduct CD4 testing to diagnose AHD in the following situations:

- Newly enrolled clients (baseline CD4) and every 6 months for unstable ART patients
- Re-enrollment after interruption in treatment
- ARV treatment failure



CD4 < 200 cells/mm³



Stage 3* or 4*



Children < 5 years old



ADVANCED HIV DISEASE

Stage 3

Most typical/common syndromes:

- Severe weight loss ($> 10\%$ of body weight)
- Chronic diarrhea for > 1 month
- Persistent fever for > 1 month
- Recurrent oral candidiasis
- Pulmonary tuberculosis
- Severe bacterial infections
- Unexplained anemia, neutropenia, or thrombocytopenia

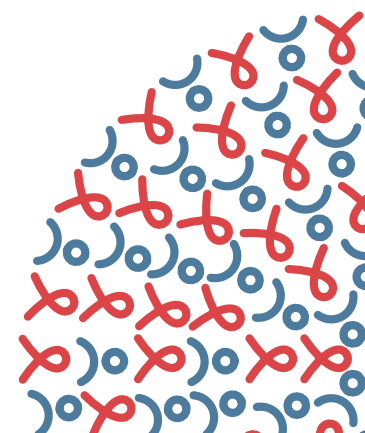
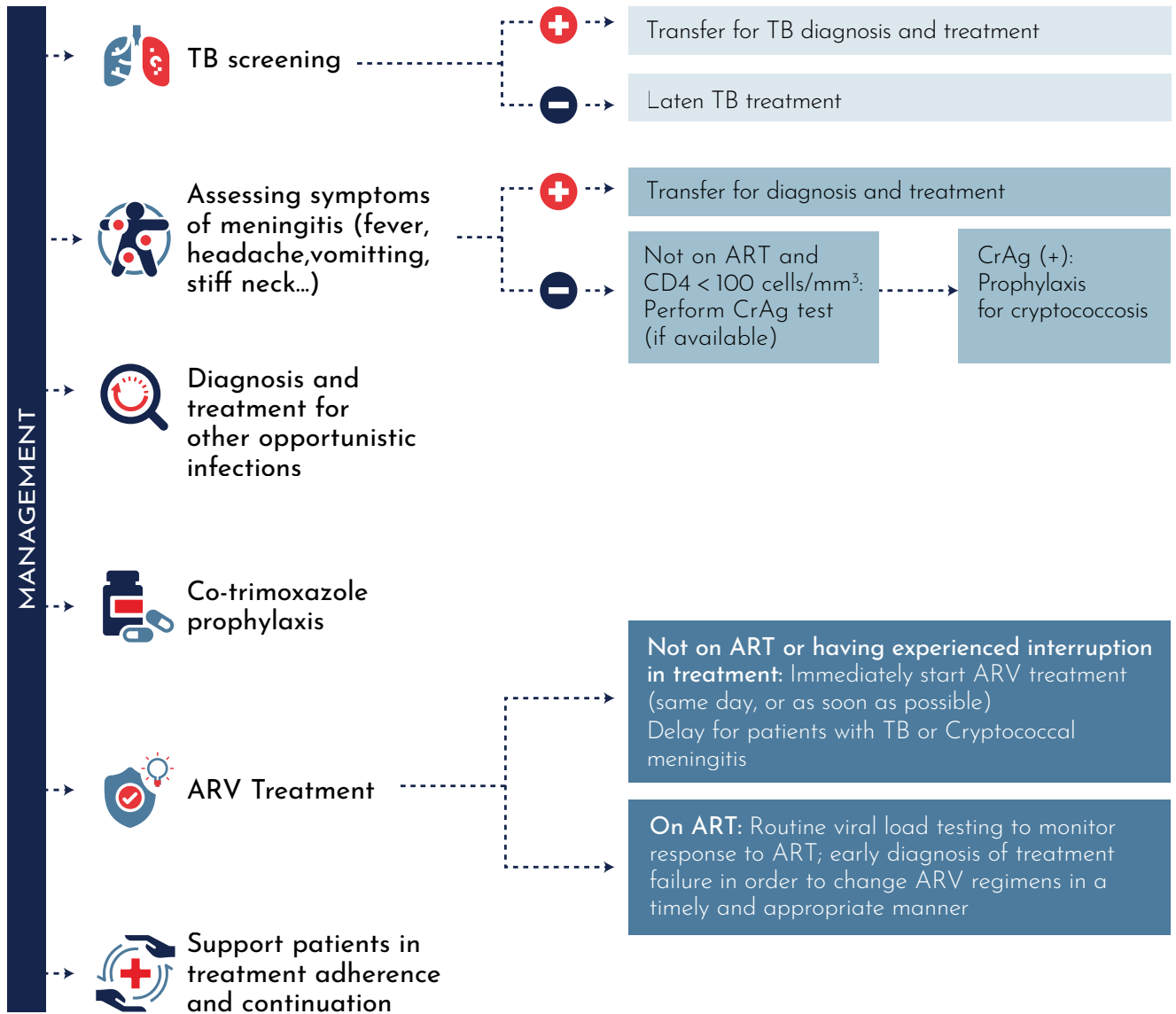
Stage 4

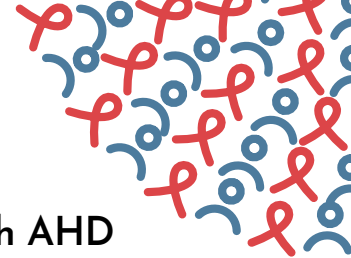
Most typical/common syndromes:

- Extrapulmonary tuberculosis
- Pneumocystis jiroveci Pneumonia (PCP)
- Esophageal candidiasis
- CNS Toxoplasmosis
- Cryptococcal meningitis
- Penicilliosis
- Persistent herpes simplex over 1 month
- CMV retinitis

2 Diagnosis and prophylaxis package of care for individuals with AHD

Provision of services for patients with AHD





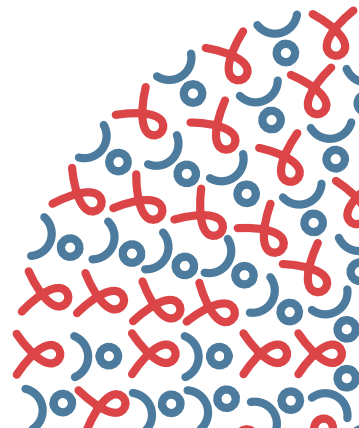
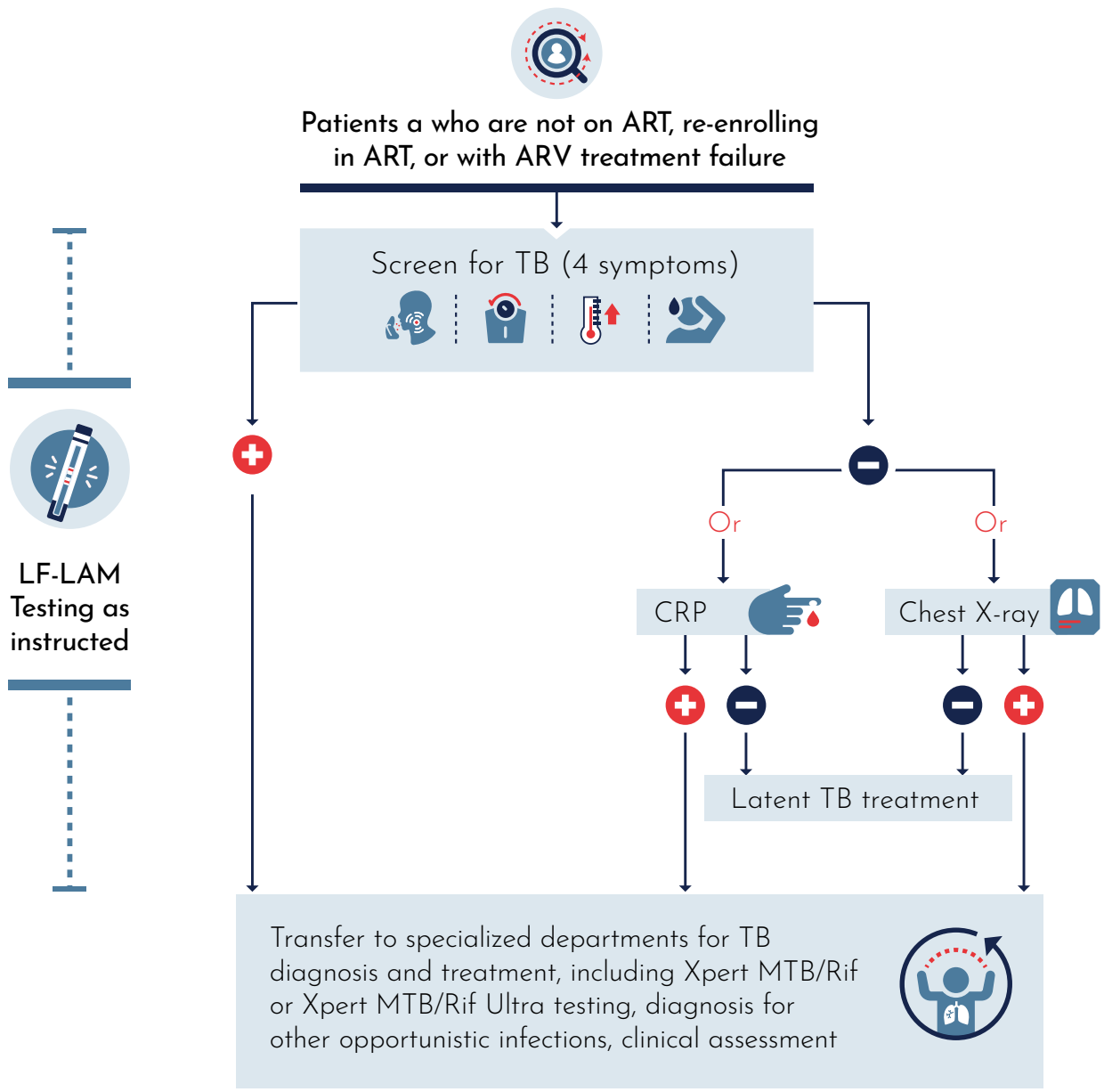
Diagnosis and prophylaxis package of care for individuals with AHD

Areas for the package	Interventions	CD4	Adults and adolescents	Children
Screening and diagnosis	When positive with 4-sign-TB screening or an abnormal chest X-ray or CRP > 5 mg/L, transfer the patient or specimen to TB unit for Xpert MTB/RIF testing for TB diagnosis	Any CD4	Yes	Yes
	LF-LAM	≤ 100 cells/mm ³ (Outpatient) ≤ 200 cells/mm ³ (Inpatient) or at any CD4 cell count value if seriously ill	Yes	Yes
	Cryptococcal antigen (CrAg) screening ¹	≤ 100 cells/mm ³	Yes	No
Prophylaxis and initial treatment	Co-trimoxazole prophylaxis	<ul style="list-style-type: none"> Adults and children > 5 years old: ≤ 350 cells/mm³ or WHO clinical stage 3 or 4 Children < 5 years old with any clinical stage or CD4 	Yes	Yes
	TB prophylaxis	Any CD4	Yes	Yes
	Fluconazole prophylaxis is preferred for CrAg-positive patients without evidence of meningitis	≤ 200 cells/mm ³	Yes	Not applicable (screening is not recommended)
ART Initiation	Rapid ART initiation	Any CD4	Yes	Yes
	Delay initiation of ART if there are suggestive symptoms of TB or cryptococcal meningitis	Any CD4	Yes	Yes
Treatment Adherence Support	Appropriate counseling to ensure treatment adherence for people with AHD	CD4 < 200 cells/mm ³ Or WHO clinical stage 3 or 4 with any CD4 Children < 5 years old with any clinical stage or CD4	Yes	Yes

1 A systematic review of 60 observational studies in 2018 found that 18.6% of individuals with CD4 counts between 100-200 cells/mm³ were CrAg positive. National guidance in Vietnam may be updated in the next revision to increase the threshold for CrAg screening in individuals with < 200 cells/mm³. (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5850628/>)

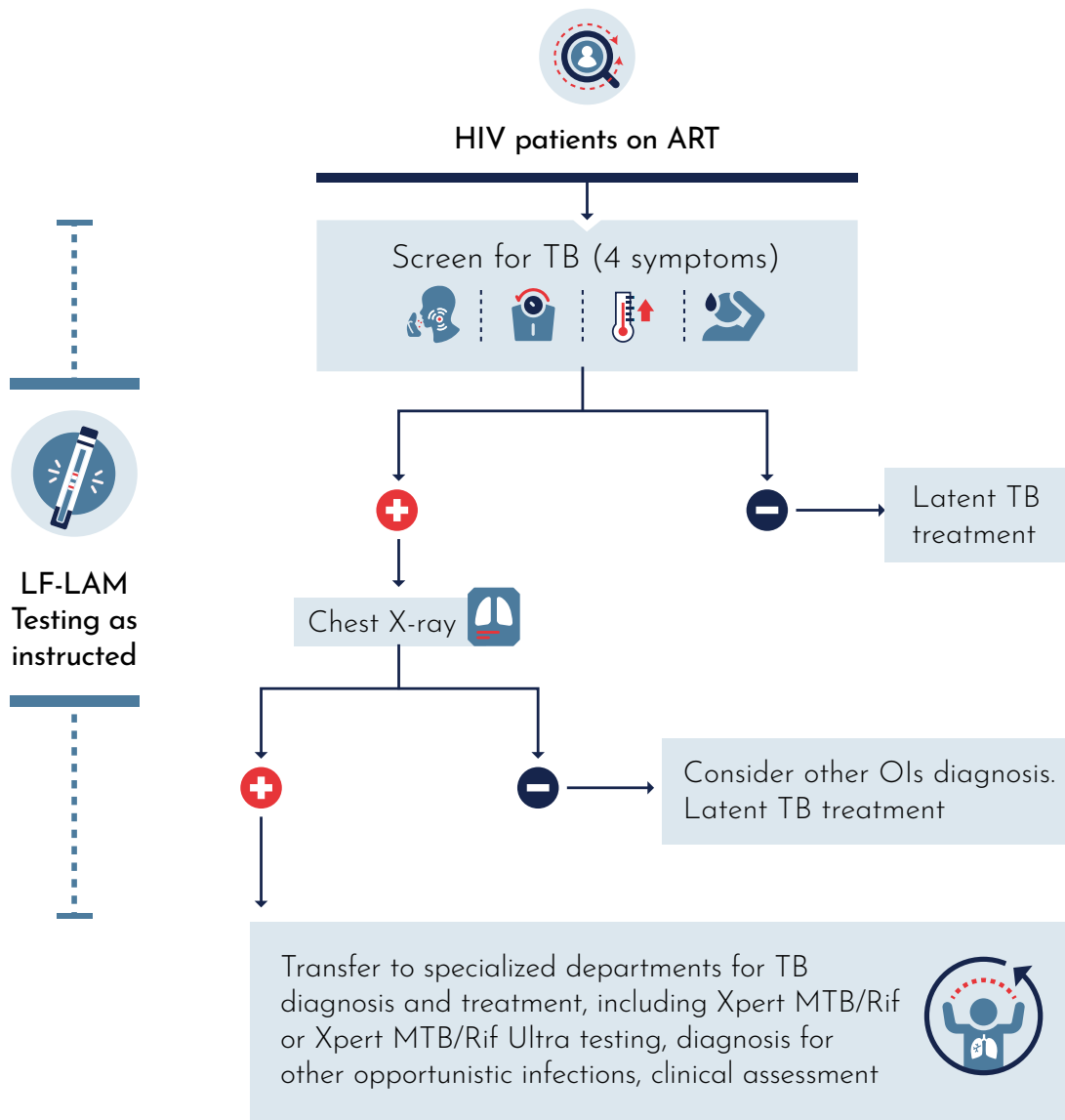
Screening and detection of TB, and treatment for latent TB

I. Screening and detection of TB in HIV outpatients who are not on ART, re-enrolling in ART, or with ARV treatment failure

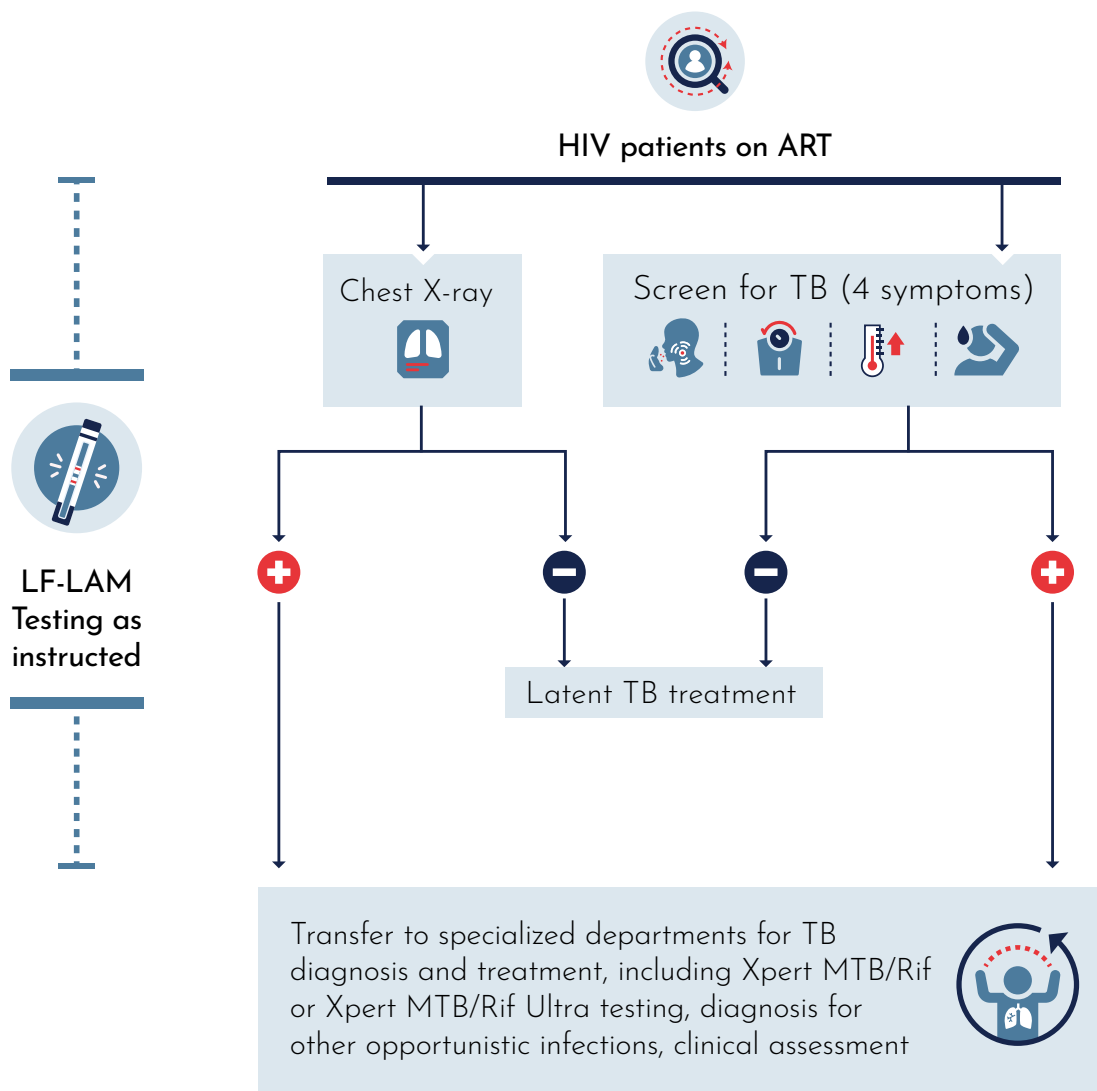


II. Screening and detection of TB in HIV outpatients on ART

1. Perform screening and detection for TB at every visit

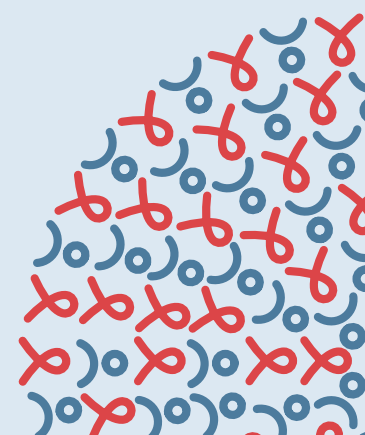


2. Screening and detecting TB at the time of Viral Load Testing

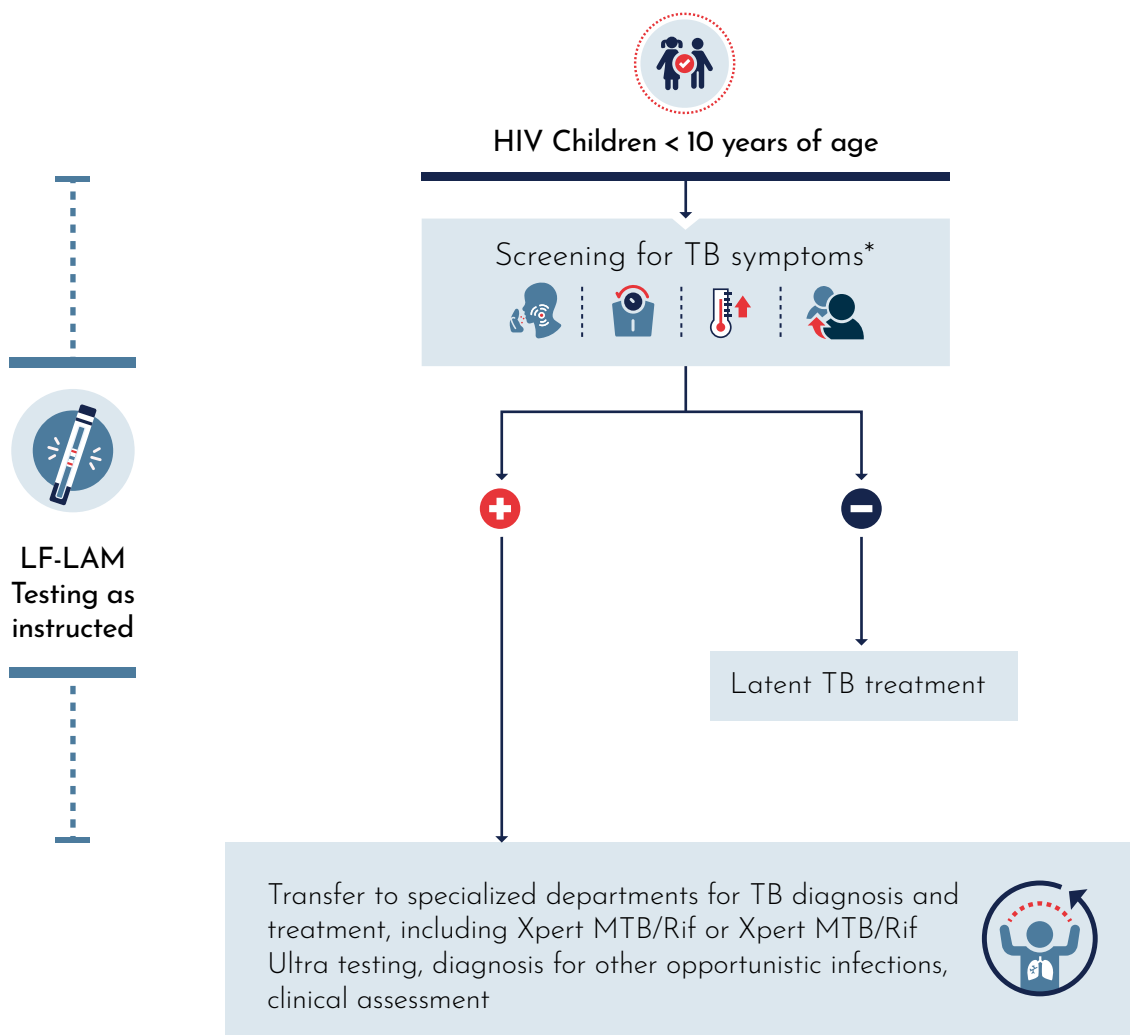


Note:

Conduct annual chest X-ray for all patients on ART whether or not they have suspected TB symptoms at the time of viral load testing

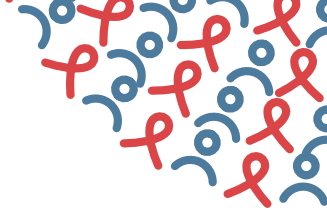


III. Screening and detection for TB among HIV children < 10 years of age



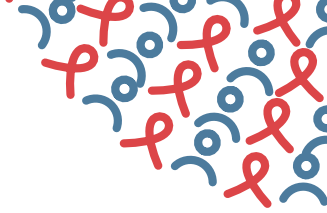
* Screening for TB symptoms in children < 10 years old:

- Cough
- Fever
- No weight gain, underweight for age, loss of body weight (> 5%) at last check, or flat growth curve
- Exposure to TB patient

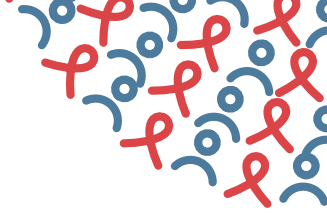


Latent TB treatment regimens

Regimen	Dose	Usage	Contraindication	Major drug interactions
6H	<p>Isoniazid:</p> <ul style="list-style-type: none"> • Patient ≥ 10 years old: 5mg/kg/day • Patient < 10 years old: 10mg/kg/old <p>Maximum dose: 300 mg/day</p>	Daily isoniazid for 6 months for adults and children	<p>History of allergy or hypersensitivity to isoniazid</p> <p>History of contact with TB patient with presumptive or confirmed rifampicin or isoniazid resistance</p> <p>Clinical symptoms of hepatitis and/or elevation of ALT > 5 times the normal range.</p> <p>Peripheral neuropathy</p>	
3HP	<p>Isoniazid:</p> <ul style="list-style-type: none"> • Patient ≥ 12 years old: 15mg/kg/week • Children 2-11 years old: 25mg/kg/week <p>Maximum dose: 900 mg/week</p> <p>Rifapentine:</p> <p>10.0 - 14.0 kg = 300 mg 14.1 - 25.0 kg = 450 mg 25.1 - 32.0 kg = 600 mg 32.1 - 50.0 kg = 750 mg > 50 kg = 900 mg</p> <p>Maximum dose: 900 mg/week</p> <p><i>(Estimated number of pills by weight, age in the table below*)</i></p>	Weekly isoniazid and rifapentine for 12 weeks for adults and children from 2 years old	<p>History of allergy or hypersensitivity to isoniazid or rifapentine</p> <p>History of contact with TB patient with presumptive or confirmed rifampicin or isoniazid resistance</p> <p>Women who are pregnant or planning to become pregnant during treatment</p> <p>Clinical symptoms of hepatitis and/or elevation of ALT > 5 times the normal range.</p> <p>Peripheral neuropathy</p>	<p>Could be coadministered with ART regimen with TDF, EFV</p> <p>No dosage adjustment required for adults when coadministered with DTG or RAL</p> <p>Should not be coadministered with PIs, NVP, TAF</p> <p>P can reduce contraceptive concentration, patients should be advised to use appropriate contraceptive methods</p>
1HP	<p>Isoniazid:</p> <p>300 mg/day</p> <p>Rifapentine:</p> <p>600 mg/day</p>	Daily isoniazid and rifapentine for 28 days. Only for some special cases requiring short-term prophylaxis and for people over 13 years old	As for 3HP	<p>Could be coadministered with ART regimen with TDF, EFV</p> <p>Should not be coadministered with PIs, NVP, TAF</p> <p>No dosage adjustment required for adults when coadministered with DTG or RAL</p> <p>R can reduce contraceptive concentration, patients should be advised to use appropriate contraceptive methods</p>



Regimen	Dose	Usage	Contraindication	Major drug interactions
3RH	<p>Rifampicin:</p> <ul style="list-style-type: none"> • Patient ≥ 10 years old: 10 mg/kg/day • Children < 10 years old: 15 mg/kg/day <p>Maximum dose: 600 mg/day</p> <p>Isoniazid:</p> <ul style="list-style-type: none"> • Patient ≥ 10 years old: 5 mg/kg/day • Children < 10 years old: 10 mg/kg/day <p>Maximum dose: 300 mg/day</p> <p><i>(Estimated dose by weight for children < 10 years old in the table below **)</i></p>	Daily rifampicin and isoniazid for 3 months for adults and children	<p>History of allergy or hypersensitivity to isoniazid or rifampicin</p> <p>History of contact with TB patient with presumptive or confirmed rifampicin or isoniazid resistance</p> <p>Clinical symptoms of hepatitis and/or elevation of ALT > 5 times the normal range</p> <p>Peripheral neuropathy</p> <p>Porphyrin metabolism disorder</p>	<p>Coadministration with TDF, EFV without dosage adjustment required</p> <p>Coadministration with R reduce DTG, RAL concentration; should double DTG dosage (50 mg/time, twice daily) and RAL dosage (800mg/time, twice daily).</p> <p>Should not be coadministered with PI, NVP, TAF</p> <p>R can reduce contraceptive concentration, patients should be advised to use appropriate contraceptive methods.</p> <p>R may interact with anticoagulants, organ transplant drugs, antidiabetic drugs, and antihypertensive drugs...</p>
4R	<p>Rifampicin:</p> <ul style="list-style-type: none"> • Patient ≥ 10 years old: 10 mg/kg/day • Children < 10 years old: 15 mg/kg/day (from 10 - 20 mg/kg/day) <p>Maximum dose: 600 mg/day</p>	Daily rifampicin for 4 months for adults and children.	<p>History of allergy or hypersensitivity to rifampicin</p> <p>History of contact with TB patient with presumptive or confirmed rifampicin resistance</p> <p>Acute or chronic liver disease with elevated liver enzymes or evidence of liver dysfunction such as jaundice... or a history of liver damage caused by rifampicin</p> <p>Porphyrin metabolism disorder</p>	<p>Coadministration with TDF, EFV is safe, no dosage adjustment required</p> <p>Coadministration with R reduce DTG, RAL concentration; should double DTG dosage (50 mg/time, twice daily) and RAL dosage (800mg/time, twice daily)</p> <p>Should not be coadministered with PI, NVP TAF</p> <p>R can reduce contraceptive concentration, patients should be advised to use appropriate contraceptive methods.</p> <p>R may interact with anticoagulants, organ transplant drugs, antidiabetic drugs, and antihypertensive drugs...</p>
6L	<p>Levofloxacin:</p> <p>Patient ≥ 15 years old:</p> <p>≤ 46 kg: 750 mg/day</p> <p>≤ 46 kg: 750 mg/day</p> <p>Children < 15 years old:</p> <p>5 - 9 kg: 150 mg/day</p> <p>10 - 15 kg: 200 - 300 mg/day</p> <p>16 - 23 kg: 300 - 400 mg/day</p> <p>24 - 34 kg: 500 - 750 mg/day</p>	Daily levofloxacin for 6 months for adults and children in close contact with MDR-TB patient.	History of contact with TB patient with presumptive or confirmed levofloxacin resistance	

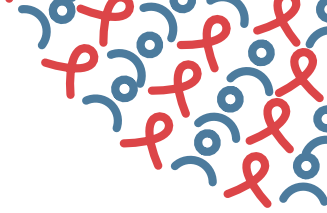


*** 3HP Dosage: Number of pills by weight and age**

From 2-14 years old	Number of pills by weight				
	10 - 15 kg	16 - 23 kg	24 - 30 kg	31 - 34 kg	> 34 kg
Isoniazid (100 mg pill)	3	5	6	7	7
Rifapentine (150 mg pill)	2	3	4	5	5
Isoniazid + rifapentine (combined pill: 150 mg/ 150 mg)	2	3	4	5	5
>14 years old	30-35 kg	36-45 kg	46-55 kg	56-70 kg	>70kg
Isoniazid (300 mg pill)	3	3	3	3	3
Rifapentine (150 mg pill)	6	6	6	6	6
Isoniazid + rifapentine (combined pill: 300 mg/ 300 mg)	3	3	3	3	3

****3RH dosage for children under 10 years old by weight**

Weight	4 -7 kg	8 - 11 kg	12 -15 kg	16 - 24 kg	>25kg
Number of combined pills (RH 75/50mg)	1	2	3	4	As for adults



Co-trimoxazole prophylaxis

Target	Criteria for initiation	Criteria for stopping	Co-trimoxazole dosage
Children exposed to HIV	All children, starting 4-6 weeks after birth	Until there's no more risk of HIV transmissions or the child is confirmed HIV-negative	In the dose of trimethoprim 5 mg/kg/day x 1 time/day
HIV-infected Children ≤ 5 years old	All children	Continuously until 5 years old	In the dose of trimethoprim 5 mg/kg/day x 1 time/day
HIV-infected Children > 5 years old	CD4 ≤ 350 cells/mm ³ or in the 3 rd and 4 th clinical stages	Clinically stable (on ARV treatment for at least 12 months and showing no signs of HIV infection in the 2 nd , 3 rd , and 4 th stages) and: HIV viral load < 200 counts/ml or CD4 > 350 cells/mm ³	Children > 30 kg: Co-trimoxazole: • 480 mg pill: 2 pills/day or: • 960 mg pill: 1 pill/day
HIV-positive adults, including pregnant and breastfeeding women	CD4 ≤ 350 cells/mm ³ or in the 3 rd and 4 th clinical stages	Clinically stable (on ARV treatment for at least 12 months and showing no signs of HIV infection in the 2 nd , 3 rd , and 4 th stages) and: HIV viral load < 200 counts/ml or CD4 > 350 cells/mm ³	Co-trimoxazole: • 480 mg pill: 2 pills/day or: • 960 mg pill: 1 pill/day

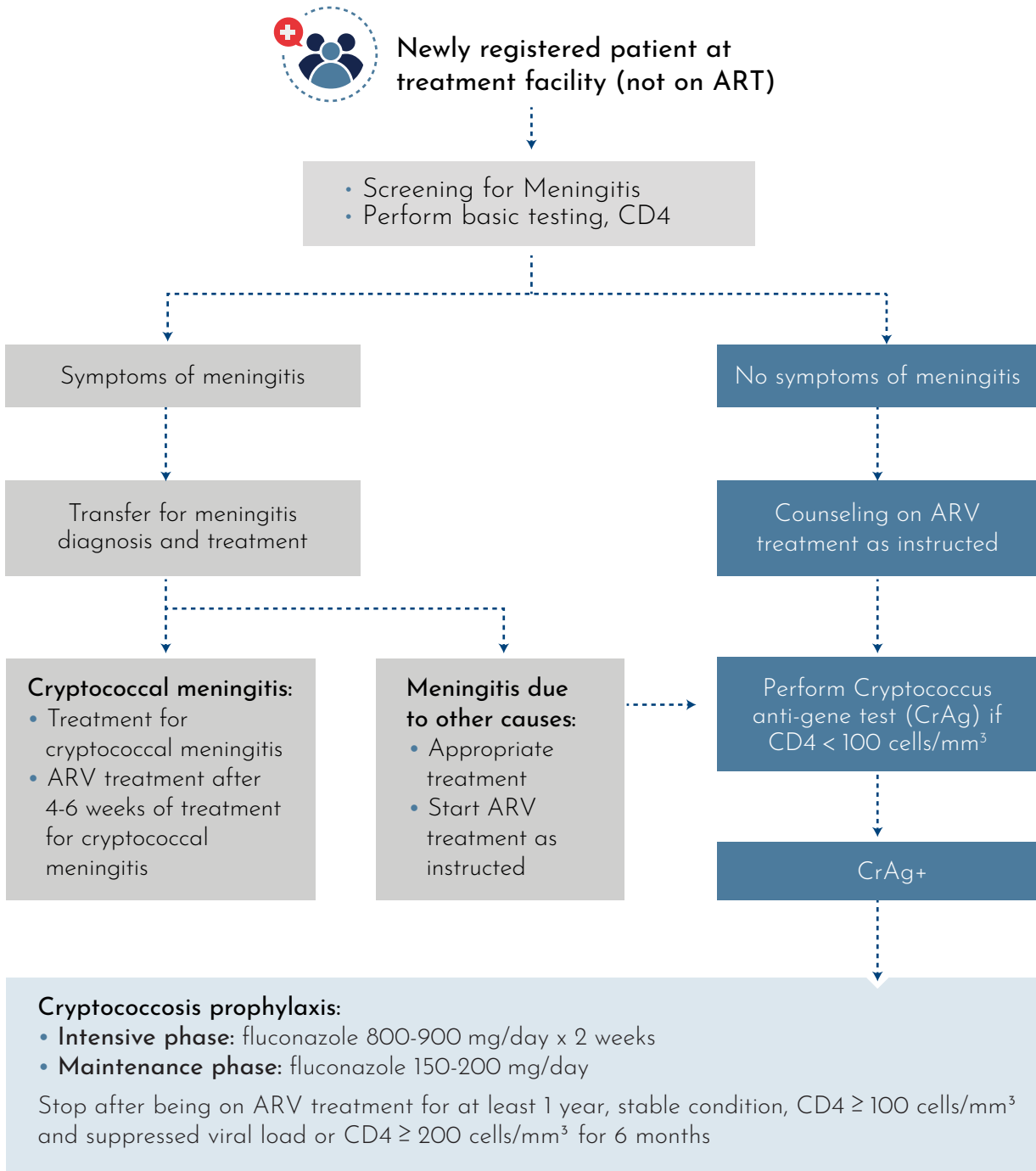
Note:

- At ART initiation, start co-trimoxazole prophylaxis for patients at clinical stage 1 or 2 without CD4 count test.
- Immediately stop co-trimoxazole if the patient shows symptoms of Stevens-Johnson Syndrome, medication allergy levels 3-4, severe liver disease, severe anemia, or severe reduction in blood cell types.

Simplified co-trimoxazole dosing for HIV-positive or HIV-exposed children

Weight (kg)	Syrup Dose: 5 mg TMP/kg/day	Pills TMP 20 mg/ SMX 100 mg x 1 time/day	Packs TMP 40 mg/ SMX 200 mg x 1 time/day	Pills TMP 80 mg/ SMX 400 mg x 1 time/day	Pills TMP 160 mg/ SMX 800 mg x 1 time/day
3.0 - 5.9	2.5 ml/time	1 pill/time	1/2 pack	1/4 pill/time	
6.0 - 9.9	5 ml/time	2 pills/time	1 pack	1/2 pill/time	
10 - 13.9	5 ml/time	2 pills/time	1 pack	1/2 pill/time	
14 - 19.9	10 ml/time	4 pills/time	2 packs	1 pill/time	
20 - 24.9	10 ml/time	4 pills/time	2 packs	1 pill/time	
25 - 34.9				2 pills/time	1 pill/time
≥ 35				2 pills/time	1 pill/time

Prophylaxis for Cryptococcosis



3 Screening for and management of common opportunistic infections in patients with AHD

Management of patients with respiratory symptoms



Patients with respiratory symptoms: cough, difficulty breathing, skin turning blue or purple... fever, weight loss

Check-up and conduct clinical assessment, basic lab test, chest X-ray

Pulmonary TB:

Progression to chronic, sub-acute, cough, fever, night sweats, X-ray scan showing abnormalities



Transfer to TB-specialized department for diagnosis and treatment

PCP: Progressive

dyspnea, dry cough, normal chest radiograph or bilateral diffuse infiltrates



Treatment with co-trimoxazole*

Transfer if needed

Bacterial pneumonia:

Acute onset, fever, wet cough, chest pain (\pm)

Chest X-ray scan:

infiltrated lung lobes



Appropriate antibiotic treatment

Transfer if needed

***PCP Treatment:**

- **Attacking phase:** Co-trimoxazole in the dose of TMP 15 - 20 mg/kg/day, 3 times/day x 21 day. If respiratory failure occurs: provide intravenous injection methylprednisolone or oral prednisolone
- **Maintenance phase (secondary prophylaxis)**
 - Adults: Co-trimoxazole 960 mg daily
 - Children: 5 mg/kg/day in the dose of TMP until on ART for at least 12 months with no sign of HIV at clinical stage 2, 3, 4 and HIV load < 200 copies/ml or CD4 count > 350 cells/mm³.
 - Do not stop prophylaxis for children under 5 years old.

Management of patients with nerve symptoms



Patients with nerve symptoms: Headache, impaired consciousness, seizures, cranial nerve paralysis, limb paralysis...

Ask for medical history; conduct clinical examination

Meningitis's symptoms: headache, vomiting, stiff neck, might be due to:

- Cryptococcal meningitis
- Tuberculous meningitis
- Bacterial meningitis

Toxoplasmic encephalitis:

Headache, localized paralysis, CT scans showing ring-shaped lesions



Transfer to specialized departments for diagnosis and treatment



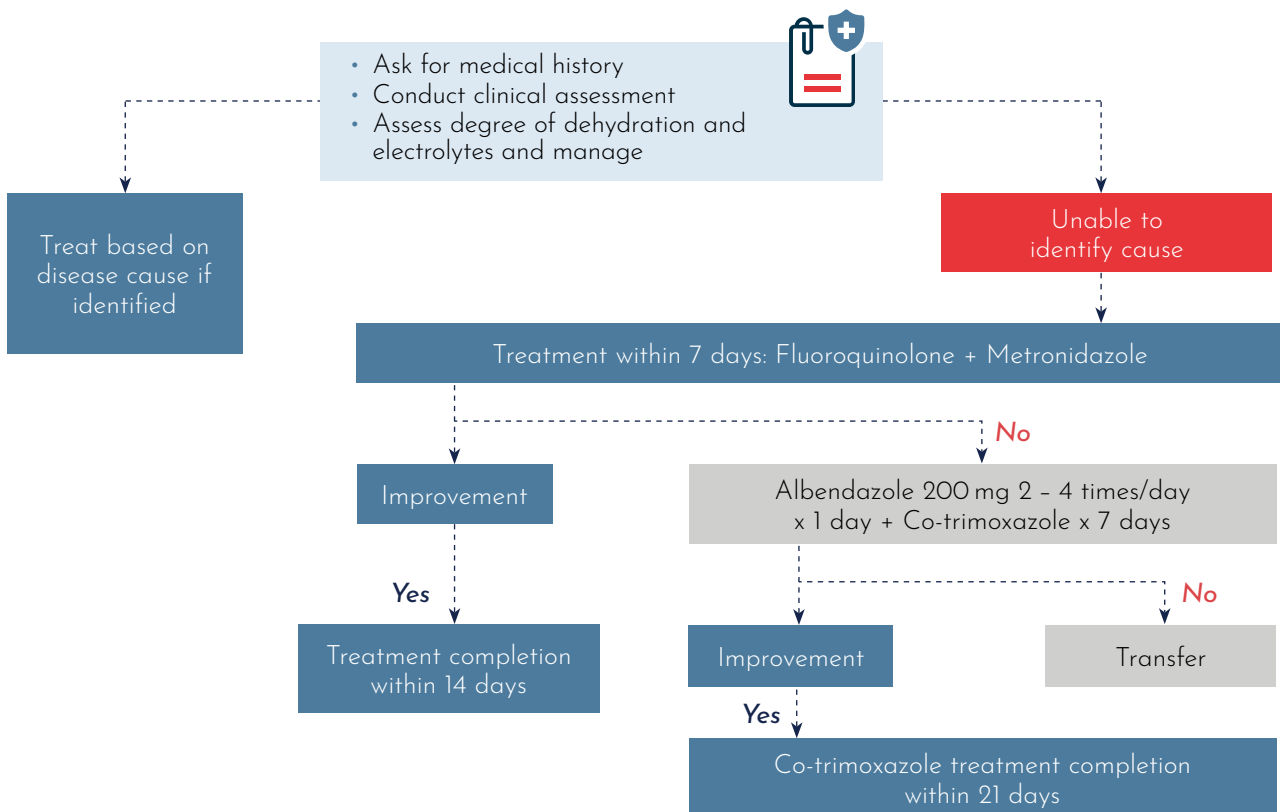
Treatment with co-trimoxazole*

Transfer to specialized departments for diagnosis and treatment

*Treatment of Toxoplasma encephalitis:

- **Attacking phase:** co-trimoxazole in the dose of TMP 10 mg/kg/day twice daily for 6 weeks
- **Maintenance phase:** oral co-trimoxazole 960 mg/day; Stop when on ART for more than 1 year, clinical stable and CD4 above 350 cells/mm³ or HIV load undetectable.

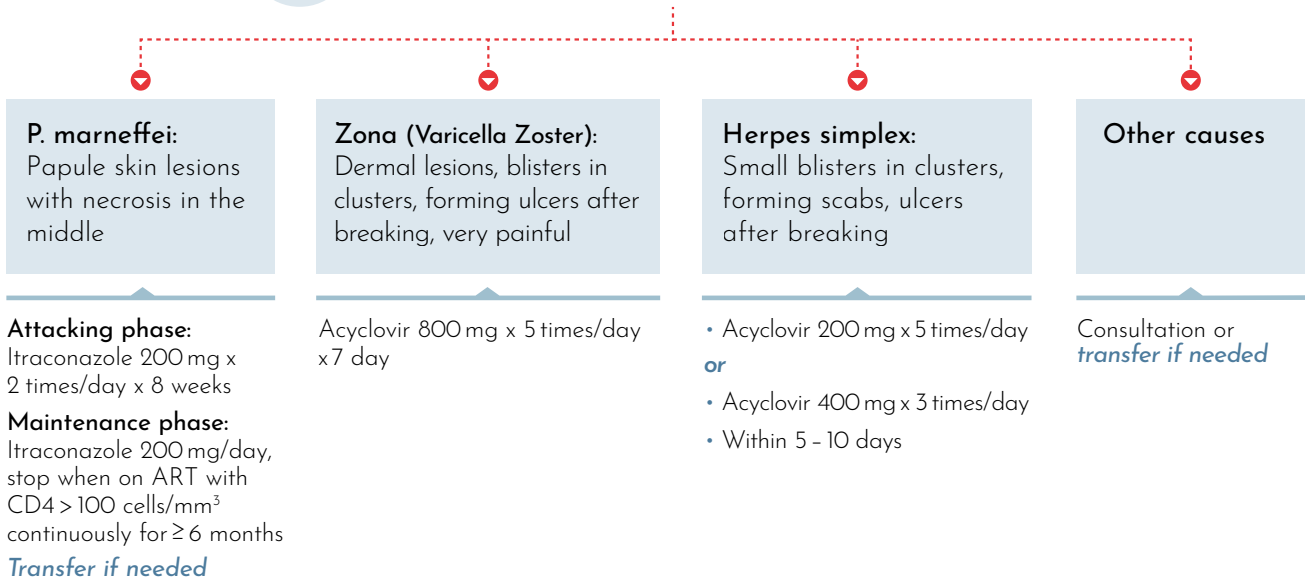
Management of patients with diarrheal symptoms



Management of patients with skin lesions



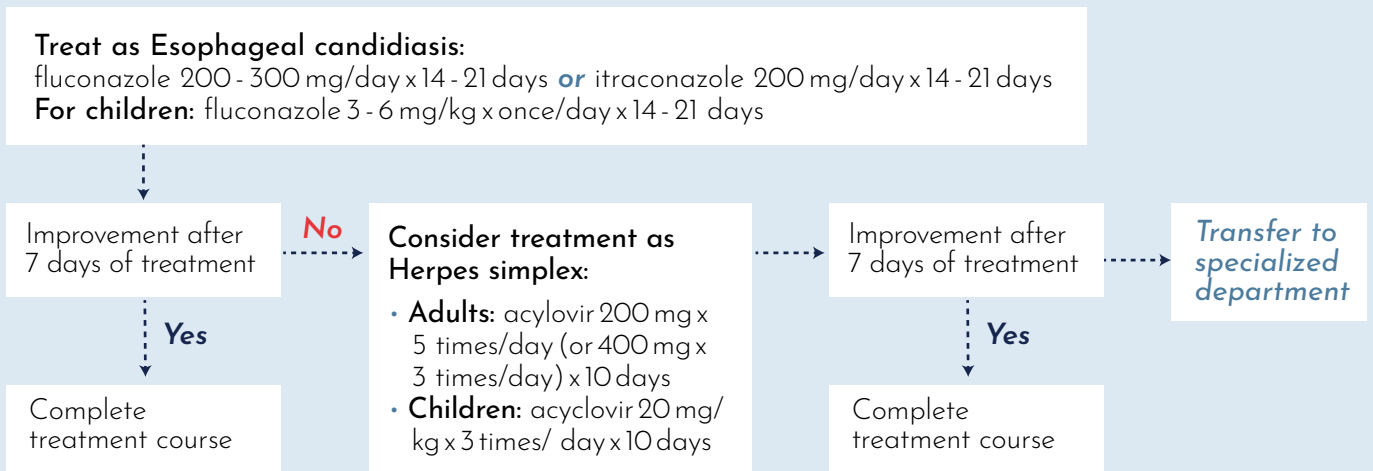
Ask for medical history; conduct clinical examination, assess skin lesions, provide clinical diagnosis



Management of patients with swallowing pains



Pain when swallowing



**Advanced HIV Disease
Management and Care**

HANOI, SEPTEMBER 2021