

Tuberculosis (TB) Screening, Diagnosis, Treatment, and Prevention in Children and Adolescents Living with HIV (CALHIV)^a



ALL CALHIV should receive as part of an initial package of care: 1) preventive therapy if there is no TB disease or 2) TB treatment if TB disease is present.

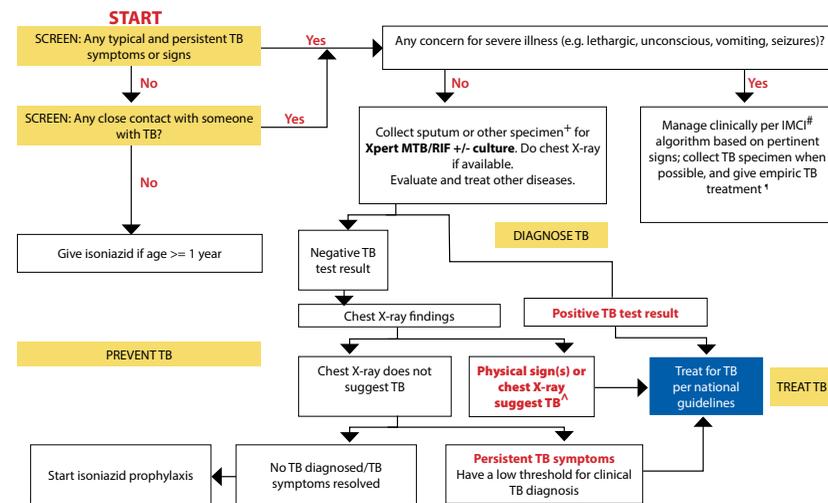
SCREEN for history of **TB contacts** and **any of these typical and persistent tuberculosis (TB) symptoms or signs at each visit:**

World Health Organization (WHO) ¹ criteria for children	World Health Organization ¹ criteria for adolescents	International Union Against Tuberculosis and Lung Disease ² criteria for children < 15 years
<ul style="list-style-type: none"> Poor weight gain^b Fever Current cough TB contact 	<ul style="list-style-type: none"> Current cough Fever Weight loss Night sweats 	<ul style="list-style-type: none"> Cough lasting longer than 2 weeks Fever that does not improve with antibiotics Weight loss or poor weight gain on growth curve Fatigue or reduced playfulness Known contact with person who has or had TB

^a HIV-exposed infants and children without known HIV status should be considered as CALHIV for the purposes of TB screening, treatment, and prevention and should be referred for HIV testing as applicable per national guidelines.

^b Poor weight gain: reported weight loss, or underweight (weight-for-age less than -2 z scores), or confirmed weight loss (>5%) since the last visit, or downward trend/flattening on growth curve.

Figure 1: TB screening, diagnosis, treatment, and prevention ¹⁻⁵



¹Other specimens include **gastric aspirate, lymph node aspirate, lumbar puncture, nasopharyngeal aspirate. Induced sputum** may also be performed. Xpert MTB/RIF should be the initial test for CALHIV.

⁴IMCI = Integrated Management of Childhood Illness (see references)

⁵WHO recommends empiric treatment for patients living with HIV and presenting with severe illness symptoms. Urine LAM may be used as a diagnostic test in those who are seriously ill.

⁶Physical signs suggesting TB include: fever, low weight, growth slowing, abnormal lung exam, cervical lymphadenopathy, abdominal swelling/ascites, spinal deformity, swelling of long bones; chest X-ray signs include hilar lymphadenopathy, focal lung opacity, cavity, miliary infiltrate, pleural or pericardial effusion.

TREAT TB

- Start TB treatment right away with isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) for 2 months followed by isoniazid and rifampicin for the duration of therapy (see Tables 1 - 5 for duration of therapy and dosing).
 - Fixed-dose combinations are recommended for children.
 - Ethambutol is considered safe for use in children at recommended dosing, thus concerns about side effects at appropriate doses should not hinder its use^{2,6}. It must be added to the fixed-dose combination.
 - Antituberculosis drugs are well-tolerated in most children; the most common side-effect is hepatotoxicity which should be suspected if a child develops liver tenderness, jaundice, or hepatomegaly⁷.
 - Streptomycin should only be used if substituted for ethambutol in tuberculous meningitis⁴.
- All CALHIV on TB treatment or isoniazid preventive treatment (IPT) should also receive pyridoxine (5-10mg/day)⁶ and cotrimoxazole.
- If no clinical improvement by four weeks of treatment, consider:
 - Poor adherence: Good adherence is important to prevent resistance.
 - Drug-resistance: Xpert MTB/RIF is used to diagnose TB in CALHIV and will detect rifampicin resistance⁵ (see drug-resistant TB section below).
 - Another disease: Generally however, TB treatment should be completed once started.
- WHO recommends that CALHIV receive 6 months of IPT for secondary prophylaxis after completing treatment for active TB disease¹.

Table 1: Duration of TB treatment⁷

Type of TB disease	Treatment phase duration	
	Intensive	Continuation
Pulmonary and extrapulmonary (excluding meningitis, bone, joint)	2 months	4 months
Meningitis, bone or joint	2 months	10 months

Table 2: NEW pediatric fixed-dose combination dispersible tablet dosing for rifampicin, isoniazid, pyrazinamide (RHZ) and rifampicin, isoniazid (RH)⁸

Weight band	Number of tablets daily		
	Intensive phase		Continuation phase
	RHZ 75/50/150 mg	Ethambutol 100mg	RH 75/50 mg
4 - 7 kg	1	1	1
8 - 11 kg	2	2	2
12 - 15 kg	3	3	3
16 - 24 kg	4	4	4
25+ kg	Adult dosages recommended		

Adapted from World Health Organization fixed-dose combination factsheet, 2015. <http://www.who.int/tb/areas-of-work/children/newdrugs/en/>

Table 3: Individual rifampicin, isoniazid, pyrazinamide, and ethambutol dosing⁷

Weight band	Number of tablets daily*			
	Rifampicin 300 mg	Isoniazid 100 mg	Pyrazinamide 400 mg	Ethambutol 400 mg
4 - 7 kg	1/4	1/2 - 1	1/4 - 1/2 [†]	1/4
8 - 11 kg	1/2	1 - 1 1/2	3/4 - 1	1/2
12 - 15 kg	1/2	1 1/2	1 - 1 1/2	3/4
16 - 24 kg	1	2	1 1/2 - 2	1
25+ kg	Adult dosages recommended			

*When ranges are specified, the lower number applies to the lower weight and the larger number applies to the higher weight.

[†]Actual dose is between 1/4 to 1/2 tablet. Dose should be approximated as is feasible.

If available, pediatric fixed-dose formulations are preferred.

Table 4: Dosing for streptomycin in addition to rifampicin, isoniazid, and pyrazinamide for TB meningitis⁶

	Dose for tuberculous meningitis only
Streptomycin	15 mg/kg once daily (range 12-18 mg/kg/day)



Figure 2: NEWLY available pediatric fixed-dose dispersible tablets on the right are an improvement over inadequate pediatric treatment formulations on the left. Photo credit: TB Alliance

Table 5: Dosing of rifampicin/isoniazid 150mg/150mg if only adult fixed-dose combination available – use along with individual pyrazinamide and ethambutol

Weight band	Number of tablets daily
	Adult fixed-dose rifampicin/isoniazid 150/150 mg
5 - 8 kg	1/2
9 - 14 kg	1
15 - 19 kg	1 1/2
20 - 24 kg	2

Drug-resistant TB

- Prevention**
 - Work with patients and families to promote adherence while on first-line regimens.
 - Good adherence to infection control measures can prevent drug-resistant TB (see the PREVENT TB section).
 - It may not be appropriate for contacts of persons with known drug-resistant TB to be given isoniazid preventive therapy as prophylaxis; consult experts in drug-resistant TB for guidance. One resource is the Sentinel Project: <http://sentinel-project.org/>, email: Sentinel_Project@hms.harvard.edu.
- Diagnosis**
 - Suspect drug-resistant TB in CALHIV who do not show clinical improvement by 4 weeks on first-line TB therapy; who have a history of prior TB disease (especially if treatment failed, was not completed, or involved poor adherence); who have been in contact with a person known to have drug-resistant TB; or have been in contact with a person suspected to have drug-resistant TB (had treatment failure, retreatment, or recently died from TB)⁷.
 - Xpert MTB/RIF should be used as the initial test to look for the presence of rifampicin resistance⁵.
 - Clinical specimens should be sent for culture and full drug-susceptibility testing if rifampicin resistance is found.
 - Attempts should be made to obtain the drug susceptibility results of any close contacts known to have drug-resistant TB, particularly because a child's specimen may be culture-negative.

- Treatment**
 - An empiric regimen for drug-resistant TB based on local epidemiology should be started as soon as possible while awaiting results of the drug susceptibility test (DST).
 - A regimen can also be constructed based on the DST of the contact(s) with drug-resistant TB.
 - When available, it is ideal to tailor the regimen to the results of the child's DST; consult an expert in drug-resistant TB for guidance.
 - Because these children are at risk for poor outcomes, closely coordinate follow-up with the TB program.

TREAT HIV

- Newly diagnosed CALHIV who have TB disease should begin antiretroviral therapy (ART) as soon as possible after tolerating TB medications and within 8 weeks after starting TB treatment (dosing in Tables 8 - 11).
- Refer to the recommended age-appropriate first line ART regimen and dosing for CALHIV and TB because of rifampicin drug interactions (see Tables 6 and 7). Once TB treatment is completed CALHIV can be switched to a standard ART regimen.

Table 6: Antiretroviral therapy (ART) regimen options for CALHIV newly initiating ART and on concurrent TB treatment (also see Tables 8-11 for specific dosing)^{4,7}.

Age group	Regimen
Child <3 years	Triple NRTIs (AZT + 3TC + ABC)
Child ≥ 3 and adolescents	2 NRTIs + EFV OR Triple NRTIs (AZT + 3TC + ABC)

Adapted from WHO 2016 antiretroviral therapy guidelines and 2014 childhood TB guidelines. NRTIs = nucleoside reverse transcriptase inhibitors, NVP = nevirapine, AZT = zidovudine, 3TC = lamivudine, ABC = abacavir, EFV = efavirenz

Table 7: Suggested changes to ongoing antiretroviral therapy (ART) regimen while on TB treatment (see Tables 8-11 for specific dosing)^{4,7}.

Age group	Recommended change options
Child <3 years	Change to triple NRTIs (AZT + 3TC + ABC) while on TB treatment only (preferred) OR
	Increase RTV dose to 1:1 equivalent dose with lopinavir (boosted PI) OR
	Increase NVP dose to 200 mg/m ² *
Child ≥ 3 and adolescents	Change to EFV OR
	Change to triple NRTIs (AZT + 3TC + ABC) OR
	Increase RTV dose to 1:1 equivalent dose with lopinavir (boosted PI)

Adapted from WHO 2016 antiretroviral therapy guidelines and 2014 childhood TB guidelines. NRTIs = nucleoside reverse transcriptase inhibitors, AZT = zidovudine, 3TC = lamivudine, ABC = abacavir, RTV = ritonavir, PI = protease inhibitor, NVP = nevirapine, EFV = efavirenz
*NVP dose calculation = 200 mg/ (√(height in cm x weight in kg)/3600).

Table 8 -11: Antiretroviral formulation dosing^{4,7}

Weight (kg)	AZT/3TC Twice daily		ABC/AZT/3TC Twice daily		ABC/3TC Twice daily		AZT/3TC/NVP + additional NVP Twice daily	
	60/30 mg tablet	300/150 mg tablet	60/60/30 mg tablet	300/300/150 mg tablet	60/30 mg tablet	600/300 mg tablet	60/30/300 mg tablet	300/150/200 mg tablet
3 - 5.9	1		1		1		1	
6 - 9.9	1.5		1.5		1.5		1.5	
10 -13.9	2		2		2		2	
14 - 19.9	2.5		2.5		2.5		2.5	
20 - 24.9	3		3		3		3	
25 - 34.9		1		1		0.5		1

Weight (kg)	LOPINAVIR/RITONAVIR (LPV/r) Target lopinavir dose 230-350mg/m ² twice daily (Add individual ritonavir to bring total dose to 1:1)			Additional ritonavir (r or RTV) for superboosting	
	80/20 mg liquid	100/25 mg tablet	40mg/10mg pellets	25 mg tablets	80mg/mL syrup
	Twice daily	Twice daily	Twice daily	Twice daily	Twice daily
3 - 5.9	1 ml		2	2	0.8 mL
6 - 9.9	1.5 ml		3	4	1.3 mL
10 -13.9	2 ml	2 in AM; 1 in PM	4	5	1.5 mL
14 - 19.9	2.5 ml	2	5	6	2.0 mL
20 - 24.9	3 ml	2	6	7	2.3 mL
25 - 34.9		3		9	2.8 mL

Weight (kg)	Additional NEVIRAPINE (NVP) to bring NVP dose to total 200 mg/m ² /per dose			EFAVIRENZ (EFV) Target dose 15 mg/kg once daily	
	10 mg/ml liquid	50 mg dispersible tablet	200 mg tablet	200 mg tablet	
	Twice daily	Twice daily	Twice daily	Once daily	
3 - 5.9	200mg/m ² /per dose	200mg/m ² /per dose	200mg/m ² /per dose		
6 - 9.9	200mg/m ² /per dose	200mg/m ² /per dose	200mg/m ² /per dose		
10 -13.9	200mg/m ² /per dose	200mg/m ² /per dose	200mg/m ² /per dose	1	
14 - 19.9	200mg/m ² /per dose	200mg/m ² /per dose	200mg/m ² /per dose	1.5	
20 - 24.9	200mg/m ² /per dose	200mg/m ² /per dose	200mg/m ² /per dose	1.5	
25 - 34.9	200mg/m ² /per dose	200mg/m ² /per dose	200mg/m ² /per dose	2	

Weight (kg)	ABACAVIR (ABC) Target dose: 8 mg/kg/dose twice daily			ZIDOVUDINE (AZT OR ZDV) Target dose: 180 -240 mg/m ² /dose twice daily			LAMIVUDINE (3TC)		
	20 mg/ml liquid	60 mg dispersible tablet	300 mg tablet	10 mg/ml liquid	60 mg tablet	300 mg tablet	10 mg/ml liquid	30 mg tablet	150 mg tablet
	Twice daily	Twice daily	Twice daily	Twice daily	Twice daily	Twice daily	Twice daily	Twice daily	Twice daily
3 - 5.9	3 ml	1		6ml	1		3ml	1	
6 - 9.9	4 ml	1.5		9ml	1.5		4ml	1.5	
10 -13.9	6 ml	2		12ml	2		6ml	2	
14 - 19.9		2.5			2.5			2.5	
20 - 24.9		3			3			3	
25 - 34.9			1			1			1

PREVENT TB

- ALL** CALHIV should be screened for active TB disease when newly diagnosed with HIV and at every clinical encounter (see Figure 3).
 - If CALHIV screen negative for TB, TB preventive therapy should be started right away if 1 year or older.
 - CALHIV who screen positive for TB but are found not to have TB should be given TB preventive therapy as soon as possible regardless of age.
- If isoniazid preventive therapy (IPT) was not previously given, a child living with HIV should be given IPT at one year of age in the absence of TB disease.
- Isoniazid preventive therapy** (10mg/kg/day – see dosing in Table 12)
 - ALL children living with HIV without active TB disease who are either ≥ 1 year or of any age and have a TB contact should be given 6 months of isoniazid along with pyridoxine (5-10mg/day)⁶. The pyridoxine dose should be increased if symptoms of peripheral neuropathy occur.
 - WHO recommends that adolescents living with HIV in high TB prevalence settings receive a minimum of 36 months of isoniazid.⁹
 - If isoniazid is not started because of ongoing work-up for suspected TB, ensure that isoniazid is started as soon as active TB has been excluded.
 - Avoid isoniazid in active hepatitis or peripheral neuropathy.
 - A history of treated TB disease does not prevent isoniazid use.
 - Monitoring for signs of TB disease should continue while a child is receiving TB preventive therapy.

- Infections control** (see WHO 2016 Consolidated Antiretroviral Drugs Guidelines – Annex 16 p.414⁴ for full infection control assessment checklist)
 - Open windows in waiting room or have open air clinics.
 - Screen all clinic patients for cough at every visit.
 - Adults and older children with cough should be triaged and separated from other patients.
 - For patients who are smear-positive, encourage them to practice cough etiquette, sleep alone, spend time outdoors, avoid congregate settings, and avoid public transportation⁴.
- Conduct TB contact investigation and provide HIV testing services for household contacts of CALHIV.
- Bacille Calmette-Guerin (BCG) vaccination.
 - BCG vaccination should not be given to infants or children with known HIV infection because of the risk of disseminated BCG disease.

Figure 3: TB screening and prevention adapted from 1⁵

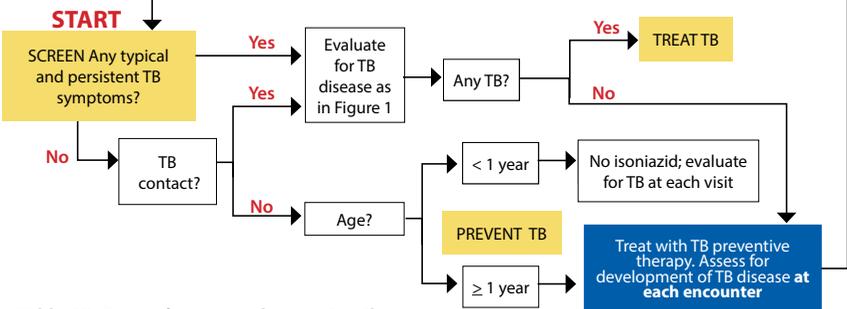


Table 12: Dosing for isoniazid preventive therapy⁴

Weight band	Number of tablets daily	
	Isoniazid 100 mg	
<6 kg	1/2	
6-9 kg	1	
10-13 kg	1 1/2	
14-19 kg	2	
20-24 kg	2 1/2	
25+ kg	Adult dosages recommended	

Resources

- Childhood TB Learning Portal.
 - http://www.unioncourses.org/online-multimedia-training-section/childhood-tb-learning-portal

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