South African National TB Guidelines - Adults

WHO STARTS TB TREATMENT?

- Patients who have bacteriological confirmation of TB: GeneXpert, AFB smear or TB culture
- Patients with clinical signs and symptoms suggestive of TB (coughing, weight loss, night sweats and/or fever) and radiological evidence with/without bacteriological confirmation

STANDARD TREATMENT OF NEW AND PREVIOUSLY TREATED TB FOR ADULTS AND CHILDREN > 8 YEARS AND > 30 KG

Pre-treatment body weight	Intensive Phase (daily for 2 months)	Continuation Phase (daily for 4 months)	
	RHZE (150/75/400/275)	RH (150/75)	RH (300/150)
30-37 kg	2 tabs	2 tabs	
38-54 kg	3 tabs	3 tabs	
55-70 kg	4 tabs		2 tabs
>70 kg	5 tabs		2 tabs
R-rifampicin, H- isoniazid, Z-pyrazinamide, E-ethambutol			

TREATMENT OF EXTRA-PULMONARY TB

- Six months treatment
- In severe forms of TB or complicated disease (meningitis, TB bones/joints, miliary TB), treatment may be extended to 9 months (2 months intensive phase (RHZE), 7 months continuation phase(RH))
- Steroids are recommended in TB meningitis and TB pericarditis – high dose steroid treatment with prednisone 1-2mg/kg daily for 4 weeks and then taper off gradually over 2 weeks

ADJUNCTIVE TREATMENT

- Pyridoxine 25 mg daily for all adult patients started on TB treatment to prevent peripheral neuropathy, may be increased to 50-75 mg (maximum of 200 mg) if no response
- Co-trimoxazole 960mg daily for HIV-infected clients

TREATMENT OF TB IN HIV CO-INFECTED PATIENTS

Patients already on ART:

- Continue ART throughout TB treatment
- EFV-based regimens are generally preferred to NVP-based regimens in adolescents and adults with active TB on 1st line ART regimens
- Patients on LPV/r and rifampicin concomitantly should have their LPV/r dose doubled slowly over two weeks (to 800/200 mg twice a day). Monitor ALT while increasing the dose at weekly intervals, and then monthly while on double dose. Continue double dose LPV/r until 2 weeks after rifampicin has been stopped
- If the patient is on an ATV/r containing regimen, then rifampicin should be replaced with rifabutin 150mg daily
- Patients on third line ARVs should be discussed with an expert or the HIV hotline for management of drug interactions

Patients not yet on ART:

- Patients who present with TB with a CD4 > 50 cells/µl, with no other serious HIV conditions (e.g. Kaposi's sarcoma or HIV encephalopathy) should start ART 2-8 weeks after starting TB treatment. If CD4 < 50, start ART within 2 weeks
- If patient is diagnosed with TB Meningitis, defer ART for 8 weeks after starting TB treatment
- If patients need to start ARV therapy and are on rifampicin, and efavirenz is contraindicated, (e.g. psychosis or previous adverse reaction to efavirenz) start nevirapine (see HIV guidelines for contra-indications to nevirapine), but do not use lead-in dose

BASELINE EVALUATION OF TB PATIENTS

All patients:

- Microscopy (AFB)
- Body Mass Index
- Height
- Urine glucose and ketones
- Weight
- Alcohol use screening

Add the following tests if the patient meets the criteria:

- Pregnancy test (women of child-bearing age, presenting with a history of amenorrhoea and not on contraception)
- HIV status (if unknown or not tested in the past year)
- Blood glucose (symptomatic patients)
- Liver function tests (history of liver disease, excessive alcohol use)
- Chest X-ray (concomitant lung disease or history of working in the mines)

NEED HELP?

Contact the TOLL-FREE National HIV & TB Health Care Worker Hotline

0800 212 506 / 021 406 6782

Alternatively send an SMS or "Please Call Me" to 071 840 1572 www.mic.uct.ac.za

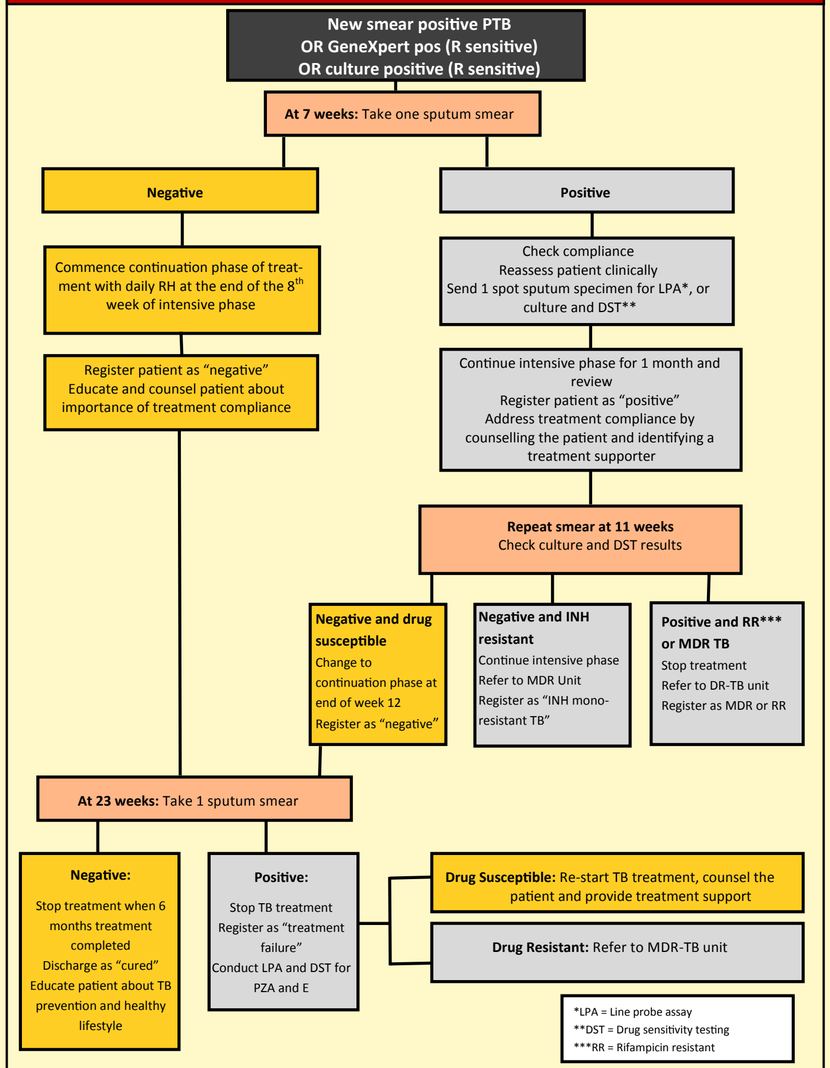
MONITORING OF PATIENTS ON TB TREATMENT

Follow-up visits: 2 weeks after start of TB treatment, then monthly

At every visit

- TB symptoms (Refer to doctor if symptoms worsen)
- Weight (Adjust dosing accordingly. If patient is losing weight, refer to doctor)
- Trace contacts and screen for TB disease. Also assess eligibility for Isoniazid Preventive Therapy in children < 5 years and HIV-infected individuals
- Discuss family planning methods
- Assess adherence by conducting pill counts, and review patient treatment cards
- Assess side-effects
- Test for HIV status if unknown
- Manage co-morbidities including HIV
- Follow-up on test results (Smear microscopy, culture, line probe assay (LPA) or drug susceptibility testing (DST), if done)

BACTERIOLOGICAL MONITORING OF PATIENTS ON TB TREATMENT



Flow chart adapted from the Aurum Institute guideline: *Managing TB in a new era of diagnostics,* 2016.

MEDICINES INFORMATION CENTRE

Based on the National Tuberculosis Management Guidelines 2014, Department of Health, South Africa

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MANAGEMENT OF COMMON ADVERSE DRUG REACTIONS TO TB DRUGS

Side effects	Drug (s) responsible	Management
Anorexia, nausea, abdominal pain	Rifampicin	Exclude drug induced liver injury/hepatitis and other causes of gastrointestinal intolerance e.g. alcohol, non-steroidal anti-inflammatory drugs (NSAIDs), gastro-oesophageal reflux, pancreatitis Take rifampicin just before or after a meal or with a light snack or at bedtime
Joint pains	Pyrazinamide	Continue TB drugs Treat symptomatically with NSAIDs Colchicine – for acute gout
Peripheral neuropathy	Isoniazid	Pyridoxine 50-75 mg daily, can increase to 200 mg daily in HIV positive patients
Orange/red coloured urine	Rifampicin	Reassure the patient
Skin itching, rash	Rifampicin, isoniazid, pyrazinamide	Depends on severity of the skin rash: • Mild, itching rash, with no blistering, mucosal involvement or systemic involvement - give antihistamine • Petechial rash - usually rifampicin. Check platelet count. If platelet count below normal range, stop rifampicin • Erythematous rash with fever, blistering, mucosal involvement, hepatitis - stop and rechallenge TB drugs once the rash resolves-should be done in hospital by an expert
Jaundice/hepatotoxicity	Rifampicin, isoniazid, pyrazinamide	Do liver function tests Exclude other causes Stop and rechallenge TB drugs in hospital
Visual impairment/loss	Ethambutol	Stop ethambutol immediately Do not rechallenge Refer to eye specialist
Thrombocytopenia/purpura	Rifampicin	Stop rifampicin and refer

TREATMENT OF TB IN SPECIAL CIRCUMSTANCES

Co-morbidity	Management
Chronic liver disease	Baseline liver function tests (LFTs) • If normal, no further LFT monitoring is required. TB treatment should be started • If LFTs are elevated but less than 2X the upper limit of normal, start TB treatment, monitor ALT monthly and assess the patient monthly for symptoms • If LFTs are elevated - greater than 2X upper limit of normal, TB treatment should not be started. Refer for further investigation and management
Acute hepatitis	Seek expert advice or phone the HIV & TB HCW Hotline
Renal impairment	Ethambutol is renally excreted. Give standard doses but prolong dosing intervals (GFR 10-50 ml/min: every 24-36 hours, GFR< 10 ml/min: every 48 hours)
Pregnancy	• Standard TB treatment is recommended. Do not exceed maximum doses • Asymptomatic infants – INH prophylaxis (10mg/kg/day) for 6 months. Defer BCG vaccination until completion of INH prophylaxis • Symptomatic infant – Treat with standard TB treatment. Defer BCG vaccination until completion of TB treatment

MANAGEMENT OF TREATMENT INTERRUPTERS

- Trace the patient
- Establish the cause for interruption of treatment
- Address the problem or concerns/counsel patient
- Collect sputum specimen for Xpert

When a patient refuses to continue treatment every effort should be made to convince the patient to continue. When all measures fail and patient insists on stopping treatment, the patient should sign a refusal of hospital treatment

DURATION OF INTERRUPTION

< 1 month	1 – 2 months		2 months or more (Lost to follow-up)	
Continue treatment and add the missed doses at the end of the treatment phase*	Continue treatment Collect sputum for Xpert and evaluate results		Do not start treatment, wait for the results Collect sputum for Xpert and evaluate results	
	Xpert positive and Rif sensitive	Xpert positive and Rif resistant	Xpert positive and Rif sensitive	Xpert positive and Rif resistant
	Continue treatment and add the missed doses at the end of the treatment phase	Stop treatment Register patient as "RR-TB" Refer to MDR-unit Do follow-up to ensure patient has been referred successfully	Register as "Treatment after loss to follow-up" Restart regimen 1	Register patient as "RR-TB" Refer to MDR-unit Do follow-up to ensure patient has been referred successfully

*Interruption during intensive phase: extend the duration of the intensive phase by the number of days the patient didn't take treatment; Interruption during continuation phase: extend the duration of the continuation phase by the number of days the patient didn't take treatment