



health

Department:
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REPUBLIC OF SOUTH AFRICA

**GUIDELINES FOR TUBERCULOSIS PREVENTIVE THERAPY
AMONG HIV INFECTED INDIVIDUALS
IN SOUTH AFRICA**

2010

TB prophylaxis

GUIDELINES FOR TUBERCULOSIS PREVENTIVE THERAPY AMONG HIV INFECTED INDIVIDUALS

Background

The dramatic spread of the HIV epidemic throughout sub-Saharan Africa in the past decades has been accompanied by up to a fourfold increase in the number of TB cases registered by national TB programmes. Strategies to control tuberculosis must now include interventions to reduce HIV infection.

On the other hand, it is estimated that around 70% of new adult cases of tuberculosis in South Africa are co-infected with HIV. Tuberculosis is the commonest cause of morbidity and mortality among HIV-infected persons in South Africa and studies have shown that tuberculosis accelerates HIV disease progression. Therefore, preventing tuberculosis among HIV-infected persons, where correctly implemented, should be offered to people living with HIV/AIDS. While TB preventive therapy may not reduce the incidence of tuberculosis in the community, it prevents morbidity and mortality attributable to TB at an individual level.

TB preventive therapy is the administration of one or more antituberculosis drugs to individuals with latent infection with *M. tuberculosis* in order to prevent progression to active TB disease.

Trials have shown that maximum benefits from TB preventive therapy are achieved in HIV-infected persons with evidence of tuberculosis infection as demonstrated by a positive tuberculin skin test. In these patients, the risk of developing tuberculosis is reduced by approximately 60% and their survival is also prolonged. However, benefit has also been shown among HIV-infected persons in general, regardless of their tuberculin test result.

TB Preventive Therapy and Health Services

TB preventive therapy is an intervention that should be part of the package of care for people living with HIV/AIDS. TB preventive therapy should only be offered if the following prerequisites have been met:

- High quality voluntary counselling and rapid testing for HIV is available.
- Patients are screened for active TB disease before initiation of TB preventive therapy.
- Providers follow up and monitor patients monthly to encourage adherence, address side-effects and exclude active TB disease.
- The HIV/AIDS programme takes responsibility for implementing TB preventive therapy.
- There is strong collaboration between HIV/AIDS and TB programmes.
- Data is collected on
 - the number of people who are started on IPT
 - The number of people who complete 6 months of IPT
 - The number of people who develop active TB when taking IPT

In order to provide comprehensive care to HIV/AIDS patients, TB preventive therapy must be rolled out to all public health services. Sites that already provide TB preventive therapy should be consulted to gain from local experience.

Exclusion of Active Tuberculosis

It is essential to exclude active tuberculosis in every patient prior to starting preventive therapy. This is critical in order to avoid giving one antituberculosis drug to patients with TB disease who require a full treatment regimen.

Prior to initiation of TB preventive therapy, patients should be screened for signs and symptoms of active TB disease:

- Current cough (24hrs or longer)
- Fever
- Loss of weight
- Drenching night sweats

All patients with 1 or more sign or symptom are considered TB suspect and must be further investigated for active TB disease as per national TB guidelines. They are not eligible for TB preventive therapy until active TB disease has been excluded on the basis of sputum smear microscopy and mycobacterial culture.

The role of chest x-ray in excluding active TB prior to initiation of TB preventive therapy remains unclear and is an additional barrier to access. Although chest x-ray is not recommended for excluding active TB disease prior to initiation of TB preventive therapy, it still has a role in working up TB suspects with negative sputum smears as per the national TB guidelines. To exclude active TB prior to initiation of TB preventive therapy, the emphasis should be on collecting sputum samples for microscopy and mycobacterial culture and, where indicated, investigations for extrapulmonary TB.

**IF THERE IS ANY SUSPICION THAT THE PATIENT HAS ACTIVE TB
THE PATIENT SHOULD NOT BE STARTED ON IPT!**

Eligibility for TB Preventive Therapy

Clinical trials have shown that the benefit of TB preventive therapy is greatest in HIV-infected persons with a positive tuberculin skin test. Where tuberculin tests are feasible and can be performed, IPT should only be offered to those who are TST positive.

However, the practicalities and logistics of doing a tuberculin skin test are often an obstacle for provision of TB preventive therapy. **Therefore the tuberculin skin test is no longer required** to identify HIV infected people eligible for IPT.

Considering the high prevalence of TB infection in South Africa, all HIV –infected people with no signs or symptoms suggestive of active TB are eligible for TB preventive therapy.

Note that the following populations are at particularly high risk of developing TB and would benefit from IPT: miners, prisoners, TB contacts, health care workers and children. Patients with signs and symptoms suggestive of TB must be investigated for TB (see flow chart). If they are found not to have TB (smear and culture are both negative), they should be reassessed in three months, and if no longer symptomatic, should be offered TB preventive therapy.

IPT and Pregnancy: yes

HIV positive TB cases cause 10% or maternal deaths in Africa. Active TB during pregnancy is associated with spontaneous abortions, and adverse perinatal outcomes.

Expert opinion is that the benefits of TB preventive therapy for eligible pregnant women, after exclusion of active tuberculosis disease, outweigh the risks. TB preventive therapy can be started at any time during pregnancy and IPT should be completed if a woman falls pregnant while taking IPT.

IPT and ART

Although ART dramatically reduces the risk of TB, patients on ART are still at increased risk of developing TB compared to HIV-negative people. The risk is highest in the first 6 months after initiating ART and often occurs in the setting of immune reconstitution inflammatory syndrome (IRIS). It is therefore critical to ensure systematic TB screening before initiating ART and during the initial 6 months of ART.

Patients who are receiving IPT and who are eligible for ART should complete their IPT while taking ART. IPT should not be stopped because they have started ART.

There is evidence that IPT is well tolerated in patients on ART. Retrospective cohort studies indicate additional benefits of providing IPT to patients during ART. Because the evidence is not based on randomised controlled trials, providing IPT to patients on ART has a conditional recommendation. Once TB has been excluded, IPT can be provided to patients during ART.

Patients on d4T and INH may be at increased risk for peripheral neuropathy and those on NVP and INH may be at increased risk for hepatotoxicity. Patients on IPT who start ART should be monitored clinically, and INH stopped immediately if there is evidence of severe peripheral neuropathy or hepatotoxicity.

IPT in patients previously treated for TB

IPT provides benefit to patients who successfully complete TB treatment. IPT can be started after successful completion of TB treatment or at any time after a previous episode of TB, provided that active TB disease is excluded.

Note that eligible patients should be counselled thoroughly

Who is Not Eligible for TB Preventive Therapy?

Patients with signs and/or symptoms of TB

Patients with active liver disease or who are actively abusing alcohol should not be offered TB preventive therapy because of the risk of hepatotoxicity .

Recommended Regimen

The standard regimen for TB preventive therapy is:

- Adults: Isoniazid (**INH**) 5 mg/kg/day (maximum **300 mg per day**).
- Children: Isoniazid (**INH**) 10 mg/kg/day (maximum **300 mg per day**).

Vitamin B6 (pyridoxine) 25 mg per day should be given concomitantly with isoniazid to prevent the occurrence of peripheral neuropathy.

The recommended duration is: **6 months of continuous treatment (can be completed over 9 months).**

If a patient has an interruption in TB preventive therapy for no more than three months, he/she can be restarted if still asymptomatic.

TB preventive therapy should be given once only. The protective effect of TB preventive therapy is expected to last for approximately 18 months.

When and How to Start

Information about tuberculosis, including preventive therapy, should be made available to all people living with HIV/AIDS. Experiences from trials and operational research have stressed the importance of relevant information for the patients including the issue of adherence. TB preventive therapy must be discussed and adequately planned to ensure full understanding and adherence by the patients. During post-test counselling following diagnosis of HIV, the patient should be informed about the benefits of TB preventive therapy, and should be invited to return to the clinic for this service. It is not recommended that TB preventive therapy be initiated immediately after informing a patient of his/her HIV status.

Among HIV-infected persons who have known their HIV status for one month or longer, a schedule is recommended as follows:

The known HIV-infected patient is screened for signs and symptoms of active TB disease. This screening is essential to exclude active tuberculosis disease that would require a full treatment regimen.

TB screening is defined as a method to intensify TB case finding among HIV+ patients. It involves asking questions about TB symptoms to identify TB suspects and to find out if the patient may have active TB. This must be done routinely by [trained] lay counselors or health care workers. The counsellor or the health worker must systematically inquire about the presence of signs and symptoms of active TB disease, as discussed above, and refer or investigate as appropriate. *See the TB screening tool at the end of the guidelines.*

Since TST is no longer essential prior to IPT, IPT can be started at the first visit if the patient is asymptomatic, well informed and willing to start IPT. If the patient is not ready to start IPT then an appointment for a second visit should be given to assess readiness to start treatment. Record the weight. In areas where TST can be done IPT should only be offered to patients who are TST positive (Mantoux induration ≥ 5 mm), but TST is not indicated if the patient is in a high risk category (miners, prisoners, TB contacts, health care workers and children)

Follow up visits:

Record the weight

During on-going counselling sessions, patients receiving TB preventive therapy will be informed about HIV, symptoms of active TB, adherence, side-effects of isoniazid (e.g. nausea and vomiting, jaundice, dark urine, right upper quadrant abdominal pain, convulsions, severe rash, psychosis and peripheral neuropathy), and the importance of immediately stopping Isoniazid and seeking care if they develop side-effects of Isoniazid.

Patients starting TB preventive therapy should be given a one-month supply at a time. They are expected to complete the 6 months of therapy within a period of 9 months. Patients should be screened for Tuberculosis at every follow up visit.

Patients who are symptomatic must be investigated according to TB guidelines:

If TB is confirmed, they should start TB treatment and receive Cotrimoxazole prophylaxis.

Eligibility for ART must be assessed.

If TB is not confirmed, they can be reassessed after three months for IPT.

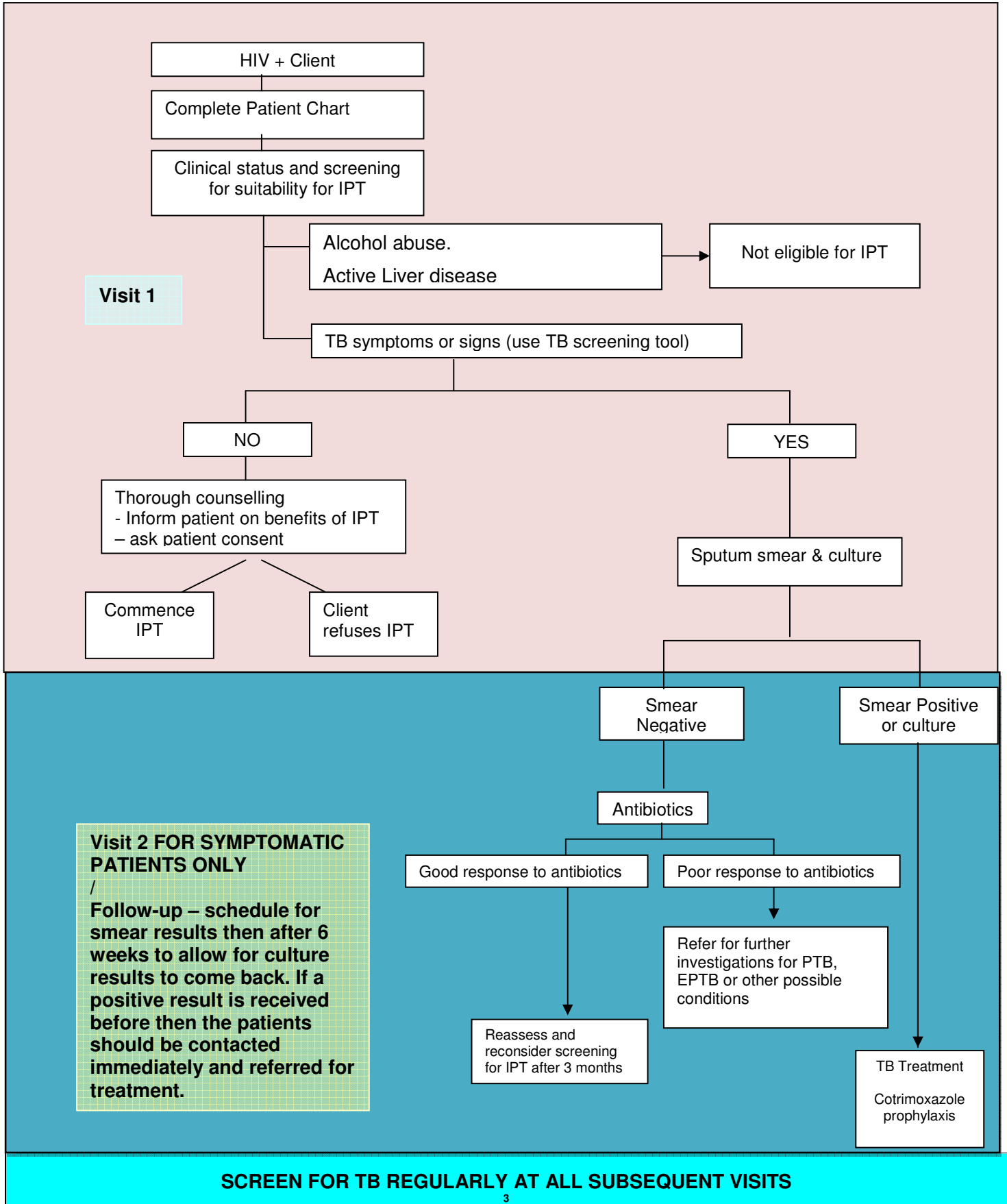
Monitoring

Patients are requested to collect their supplies on a monthly basis. This visit is also an opportunity for on-going counselling, identification of side-effects (e.g. nausea and vomiting, jaundice, dark urine, right upper quadrant abdominal pain, convulsions, severe rash, psychosis and peripheral neuropathy)), and early detection of active TB. Patients should come for review if any symptoms of active TB disease or side-effects of isoniazid occur.

- **Screen for TB symptoms at every visit:** If the patient develops symptoms of active TB, preventive therapy, investigations should be CONTINUED, and the patient should be investigated for active TB disease. A full TB treatment regimen should be started if active TB is confirmed.
- Check for side effects:
 - In cases of mild **peripheral neuropathy**, vitamin B6 (pyridoxine) must be increased from 25 mg to 100 mg daily until the symptoms disappear. If the peripheral neuropathy is severe or worsens, then Isoniazid should be discontinued immediately.
 - If the patient develops signs or symptoms suggestive of **hepatitis**, isoniazid should be stopped immediately, blood should be sent for liver function tests (an ALT is adequate), and the patient should be referred immediately to a medical officer.
- **Monitor adherence:** If the patient interrupts therapy, the healthcare provider should inquire about the reasons for treatment interruption, and should counsel the patient on the importance of adherence. Isoniazid may be restarted after the healthcare provider has verified that the patient has no symptoms suggestive of active TB disease, and that obstacles to adherence have been addressed. The healthcare provider should make sure that the 6 months of therapy is taken within a 9 month period. If the patient interrupts TB preventive therapy for a second time, the healthcare provider should consider stopping the therapy.

TB preventive therapy has been shown to benefit HIV-infected individuals. It does not aim to control TB on a population level, and it is not an alternative to the DOTS strategy for controlling TB. It is a very effective intervention for preventing morbidity and mortality attributable to TB among HIV-infected individuals.

Figure 8: Screening Algorithm for TB Prophylactic Therapy (PT)



Recommendations for implementation plan

Pre-conditions:

- The HIV/AIDS programme takes responsibility for implementing TB preventive therapy.
- High quality voluntary counselling and rapid testing for HIV is available.
- Patients are screened for active TB disease before initiation of TB preventive therapy.
- Providers follow up and monitor patients monthly to encourage adherence, address side-effects and exclude active TB disease.
- There is strong collaboration between HIV/AIDS and TB programmes.

Planning

- Province to agree on objectives and policy and inform the district and health facilities
- Identify who is responsible / the champion
 - At district and sub-district levels
 - At facility level
- Identify sites where IPT is already implemented and gather lessons for implementation in other sites
- Identify needs (advocacy campaigns and IEC materials, training, supplies, RR and M&E, etc)
- Define roles: Who is responsible?
 - To inform all relevant stakeholder and provide information (managers, HIV/VCT/PMTCT/TB/PHC coordinators, NGOs, PLWHA groups)
 - To develop and implement an advocacy campaign/PLAN
 - To develop an implementation plan
 - To provide IPT including: patient info, TB screening, INH prescription, adherence support (counsellors, nurses, pharmacist, doctors, data clerks, coordinators, NGOs...)
- Decide sites (start with performing ones where support and/or mentoring is well established), Time frames and M&E
- Advocacy, Communication, Social Mobilisation
- Monitoring: Data is collected on
 - the number of people who are started on IPT
 - The number of people who complete 6 months of IPT
 - The number of people who develop active TB when taking IPT



TUBERCULOSIS SCREENING TOOL FOR ADULTS

Surname _____ First Name _____

Address _____

Contact number _____

Date _____

Patient record or Folder Number: _____

Reason for screening:

TB contact

MDR/XDR TB Contact

HCT/PMTCT/VCT/CCMT/ART

Answer "yes" or "no" on the following questions

Symptoms	Yes	No
Do you have a cough (24 hours or more)?		
Do you have loss of weight?		
Do you sweat a lot at night?		
Do you have fever?		

If "yes" to one or more of the questions, suspect TB

Clinically evaluate the patient using national guidelines for diagnosing TB. If required refer for further investigations including a sputum for microscopy and culture

If "no" to all questions, inform the patient on the benefit of IPT (TB preventive therapy) and assess patient eligibility or refer the patients for IPT eligibility

	Yes	No
TB Suspect?		
Sputum collected?		
IPT started / referred for IPT		

Patients referred to the clinic _____

Name of counsellors / health care worker _____

Facility / contact details _____