Hey there, my name is **Isoniazid Preventative Therapy**

You may call me IPT. My power includes helping to reduce the risk of active TB developing in those friends who are living with HIV, by targeting my spear at TB, while it is still sleeping in their bodies. Find out more about how I am able to reduce the risk of TB disease (in people living with HIV) by 33 - 67%, for up to 48 months...
What is TB chemoprophylaxis and why is it recommended in people living with HIV? What drug is used for TB chemoprophylaxis?

TB chemoprophylaxis (also known as Isoniazid preventive therapy IPT) is giving anti-TB drugs to PLHIV with latent TB infection to kill off the bacteria before it develops into active disease. The provision of IPT to PLHIV does not increase the risk of developing Isoniazid (INH) resistant TB. The drug being used for IPT is INH at 300mg/day. Many studies around the world have shown that IPT reduces the risk of TB disease by 33%-67% in people living with HIV for up to 48 months.

What is the optimal duration of IPT?

It is recommended that IPT be given for 6 months to adults (including pregnant women), children, PLHIV, those receiving ART and those whose TB treatment has been successful. In places with a high number of people infected with HIV and TB however, the WHO has recommended providing IPT for 36 months (or as a life-long treatment).

How long does the protective value of IPT last? Should repeated courses of IPT be administered?

The protective benefit of IPT ranges from 6 months to 5 years. The loss in protective benefit could be due to the high prevalence of TB in the community and re-infection or within high risk populations including health care workers, household contacts of TB patients, prisoners, and miners. Despite the loss in the protective benefit, current recommendations are for a single daily dose of IPT to be given for 6 months because of concerns with lifelong or periodic treatment with IPT that include risks of the development of toxicity or high costs. However two recent clinical trials track a benefit of IPT treatment for 36 months or longer, especially for those who are TST positive.

How important is adherence to IPT?

Various studies have shown that adherence rates for IPT vary significantly from 34%-98%. However, there is no data indicating that poor adherence, results in adverse outcomes such as resistance to isoniazid. WHO Guidelines emphasise that concerns about adherence should not hinder IPT implementation. It is reported that adherence could be enhanced by co-formulation of INH with other drugs such as ART or Co-trimoxazole Prophylaxis (CPT), reducing the pill burden. While adherence to IPT is important for the prevention of active TB, the more important focus for patients on IPT should be on regular clinical follow up, prompt evaluation for TB if symptoms appear and/or stopping IPT if signs of toxicity appear. A critical and overlooked factor is data capturing tools for patients who are on IPT which allows for ease of monitoring and evaluation of patients and programme performance.

41 Ibid P 10
42 Ibid P 11
19 Is it safe to administer IPT together with ART?

Isoniazid has potential adverse effects, including nausea, vomiting, rash, fever, hepatitis, and peripheral neuropathy. Hepatotoxicity, sometimes severe and even fatal, has been found in a very small proportion of individuals receiving isoniazid treatment. It is important to inform clinicians and patients about this possibility and be aware of the signs and symptoms of hepatitis, especially if the person taking IPT has other risk factors for liver disease such as regular alcohol consumption. Among patients receiving both ART and IPT, the risk of peripheral neuropathy is increased if stavudine or didanosine is used, although the addition of vitamin B6 (pyridoxine) may prevent peripheral neuropathy. Studies in South Africa suggest increased risk of liver toxicity. Symptoms of early hepatitis infection include decreased appetite, fatigue, abdominal pain, nausea, vomiting, jaundice, itching, and flu-like symptoms. When using IPT it is important to provide patients with careful counselling, clinical monitoring, and good patient education regarding when to stop treatment and seek advice so as to reduce the risk of toxicity.

20 Does IPT have any added benefit in people whose immune systems are already strengthened by ART?

Even though ART reduces the incidence of TB infection, TB incidence rates remain high in HIV-infected patients. The use of both IPT and ART in HIV-infected patients has been shown to significantly reduce tuberculosis incidence. A study on the effects of using IPT with ART found that while patients receiving ART had a 64% reduced risk for tuberculosis, patients receiving ART after IPT had an 89% reduced risk. Therefore, it is recommended that IPT be given regardless of whether a patient is on ART. In addition, being on IPT should not delay starting ART in eligible people living with HIV, such as those without active TB. A separate study affirmed that administering ART with IPT reduces the chances of TB infection. And people on effective ART may be able to take IPT “intermittently, every second or third year” due to effects of IPT being longer than previously hypothesised.

21 Is it safe to administer IPT together with ART?

IPT should be provided to patients regardless of CD4 count. The REMEMBER trial is a multicountry study that compares the provision of ART and TB treatment with ART and IPT in people with HIV with a CD4 count below 50 cells/mm3 and presumed not to have active TB. The trial showed no evidence of reduced mortality, reduced incidence of AIDS-associated illnesses or increased viral suppression as a result of presumptive therapy in individuals in whom TB was not suspected and in whom it had been ruled out by extensive investigations.

Does IPT increase the risk of isoniazid resistance in people with latent tuberculosis?

IPT is only recommended for patients with latent tuberculosis and it is very important that a patient does not have active TB disease when given IPT. If active TB develops, which rarely occurs while on IPT, IPT should be stopped.\textsuperscript{50} It is important to thoroughly screen people for TB symptoms to eliminate the possibility of active TB before beginning IPT. In individuals with latent TB, few bacilli exist in the lungs which are slowly dividing, making the likelihood of developing drug resistance low. There is still a slight possibility that the use of isoniazid alone for the treatment of latent TB infection may result in isoniazid resistance. However, this should not prevent the use of IPT amongst those living with HIV. The WHO recommends regular TB screening for those taking IPT in order to help identify those who develop active TB.

Is IPT safe in pregnant women?

The existing evidence suggests that IPT is safe in pregnant women.\textsuperscript{51} It is recommend that pregnancy should not exclude women living with HIV from symptom based TB screening and receiving IPT.

When is IPT not recommended for patients?

Patients with active TB should not be put on IPT. Individuals with active hepatitis (acute or chronic), regular and heavy alcohol consumption and symptoms of peripheral neuropathy are also not recommended to start IPT. However, past history of TB and current pregnancy should not prevent initiation of IPT.

Can IPT be administered safely in children? How would active TB be excluded in children?

IPT is an important intervention for preventing and reducing tuberculosis amongst people living with HIV. IPT is proven to be effective and safe in both adults and adolescents as well as children. The algorithm for screening HIV-infected children older than one year is the same as the algorithm for screening adults. All available data suggest that INH is not toxic for children, even in those receiving ART. HIV-infected children, over one year of age who present with no evidence of active TB (weight loss, fever, night sweats and current cough), despite the availability of contact history, should be given IPT. IPT in children should be given at a dose at 10mg/kg/day for 6 months (not to exceed a maximum daily dose of 300mg). Simultaneous administration of vitamin B6 25 mg daily is recommended, to prevent neuropathy.

Is IPT recommended for PLHIV with MDR/XDR TB after they are successfully treated?

The use of IPT in patients who have successfully completed treatment for MDR or XDR TB is not recommended.

\textsuperscript{51} Ibid