Revised National TB Control Programme

Technical and Operational Guidelines for Tuberculosis Control in India 2016

Central TB Division, Directorate General of Health Services
Ministry of Health & Family Welfare, New Delhi, India
www.tbcindia.gov.in
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Preface

The first technical & operational guidelines for Revised National TB Control Programme (RNTCP) were developed during the initial years of implementation of the programme & were updated in 2005. The current document outlines the guidelines on TB care in line with RNTCP National Strategic Plan for Tuberculosis Control 2012-17.

These guidelines were conceived by programme managers working at the national, state and district levels. Experts from national institutes, national and intermediate reference laboratories, medical colleges and partners were involved in the process of preparing it.

Standards for TB Care in India, National Strategic Plan document, Recommendations of the Joint Monitoring Mission 2012 and policy decisions taken in the National Committee on Diagnosis and Management of Tuberculosis under RNTCP, National Technical Working Group on TB-HIV, National Technical Working Group on Pediatric TB, Expert committee on regulation of newer anti-TB drugs were used as a foundation for developing this document. Existing technical and operational guidelines, training module for medical officers, National PMDT guidelines, National Air borne infection control guidelines, Revised pediatric TB guidelines, National guidelines on partnerships, Guidelines for Quality Assurance of smear microscopy for diagnosing tuberculosis, National Framework for Joint HIV/TB Collaborative Activities and Guidelines for use of Bedaquiline in RNTCP through conditional access under programmatic management of drug resistant TB in India have also been referred.

The document covers strategies and guidelines for diagnosis and treatment of all forms of TB including pulmonary, extra-pulmonary, drug resistant TB, TB with comorbidities, pediatric TB, etc. Programme management aspects covering patient support systems, human resource management, partnerships for TB control, advocacy, communication and social mobilization, infection control measures, planning and finance are also incorporated.

These technical and operational guidelines are intended to be used by all the personnel engaged in control of TB in the country. This is a living document open to further improvements and will be updated as lessons are learned through its use in the field.
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Introduction

Tuberculosis

Tuberculosis (TB) is an infectious disease caused predominantly by *Mycobacterium tuberculosis*. Tuberculosis is most commonly transmitted by inhalation of infected droplet nuclei which are discharged in the air when a patient with untreated TB coughs or sneezes. TB disease usually affects the lungs, but can involve any part of the body. Pulmonary TB which affects lungs is an infectious form of disease. Extra-pulmonary TB can affect the lymph nodes, pleura, bones and joints, the genito-urinary tract, the nervous system (meningitis, tuberculoma), abdominal TB (intestines, mesentry, solid organs), skin, etc. All those who get infected do not necessarily develop TB disease. The life time risk of breaking down to disease among those infected with TB is 10–15%, which gets increased to 10% per year amongst those co-infected with HIV. Other determinants such as diabetes mellitus, smoking tobacco products, alcohol abuse and malnutrition also increase the risk of progression from infection to TB disease.

Burden of TB

India accounts for one fourth of the global TB burden i.e. 2.2 million out of 9.6 million new cases annually. In India, more than 40% of population is infected (prevalence of infection) with *Mycobacterium tuberculosis*. It is estimated that there are 2.5 million prevalent cases of all forms of TB disease. It is also estimated that about 2.2 lakhs people die due to TB annually (mortality). The table below shows the estimated figures for TB burden globally and for India provided by WHO for the year 2014.

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<tr>
<th></th>
<th>Incidence</th>
<th>Prevalence</th>
<th>Mortality</th>
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<tr>
<td>Global</td>
<td>9.6 million</td>
<td>13 million</td>
<td>1.1 million</td>
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<tr>
<td></td>
<td>(176/lakh/year)</td>
<td>(227/lakh/year)</td>
<td>(21/lakh/year)</td>
</tr>
<tr>
<td>India</td>
<td>2.2 million</td>
<td>2.5 million</td>
<td>2.2 lakhs</td>
</tr>
<tr>
<td></td>
<td>(167/lakh/year)</td>
<td>(195/lakh/year)</td>
<td>(17/lakh/year)</td>
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*Source: Global TB Report 2015*

TB now ranks alongside HIV as a leading cause of death worldwide. TB kills more adults in India than any other infectious disease.

In India, every day:

- more than 6000 develop TB disease
- more than 600 people die of TB (i.e. 2 death every 5 minutes)

India has highest burden of both TB and MDR TB and second highest of HIV associated TB based on estimates reported in Global TB Report 2015. An estimated 71,000 cases of MDR-TB emerge annually from the notified cases of pulmonary TB in India. Based on sub-national DR surveys carried out in three states of India, ~3% among new TB cases and 12%-17% among previously-treated TB cases have MDR-TB. India bears second highest number of estimated HIV associated TB in the world. An estimated 1.1 lac HIV associated TB occurred in 2014 and 31,000 estimated number of patients died among them.
TB control strategy

The National Tuberculosis Programme of India (NTP) was initiated in 1962 and was originally designed for domiciliary treatment, using self-administered standard drug regimens. The NTP had created an extensive infrastructure for TB control with a network of more than 446 District TB Centres, 330 TB clinics and more than 47,600 TB beds. The NTP had also raised the awareness of TB and TB treatment facilities, and had succeeded in placing more than 1.3 million patients on treatment annually. Despite the NTP being in existence since 1962, no appreciable change in the epidemiological situation of TB in the country had been observed. The HIV/AIDS epidemic and the spread of multi-drug resistance TB were threatening to further worsen the situation.

In view of this, in 1992, GoI, with WHO and SIDA reviewed the TB situation and the performance of the NTP. The observations revealed that the NTP, though technically sound, suffered from managerial weaknesses, inadequate funding, an over-reliance on X-Ray for diagnosis, had frequent interrupted supplies of drugs, and low rates of treatment completion. The Government decided to give a new thrust to TB control activities by revitalising the NTP, with assistance from international agencies. In 1993, the Revised National TB Control Programme was piloted in a population of 2.4 million in five states. This was later expanded to cover 13 million people by 1995, and 20 million by 1996.

In 1997, the RNTCP was launched as a national programme with a plan to scale up in a phased manner. The RNTCP thus formulated, adopted the internationally recommended Directly Observed Treatment Short-course (DOTS) strategy, as the most systematic and cost-effective approach to revitalise the TB control programme in India. Political and administrative commitment to ensure the provision of organised and comprehensive TB control services; reliable and early diagnosis through smear microscopy of self-reporting chest symptomatics in the general health services; an uninterrupted supply of good quality anti-TB drugs through patient wise boxes (PWBs); effective and patient-friendly treatment with SCC given under direct observation; and accountability through proper recording and reporting, and effective supervision were emphasised.

The objectives of the RNTCP were to achieve at least 85 percent cure rate among the new smear-positive cases initiated on treatment, and thereafter a case detection rate of at least 70 percent of such cases. The RNTCP was built on the infrastructure and systems built through the NTP. Major additions to the RNTCP, over and above the structures established under the NTP, was the establishment of a sub-district supervisory unit, known as a TB Unit, with dedicated RNTCP supervisors posted, and decentralization of both diagnostic and treatment services, with treatment given under the support of DOT providers. The entire country was covered by the end of 2005. The programme has made rapid strides ever since its implementation. The programme has consistently been achieving global benchmarks of case detection and treatment success rates since 2007.

The widespread implementation of the DOTS strategy has proved to be an effective tool in controlling TB on a mass scale and practiced in over 200 countries. The prime task for the next
decade was to achieve the Millennium Development Goals (MDGs) and related STOP TB Partnership targets for TB control. The target under MDG for tuberculosis is to halt and begin reversal of incidence of tuberculosis, malaria and other major diseases by 2015. The indicators were to reduce the prevalence and death rates by 50% between 1990 and 2015.

Meeting these targets required a coherent control strategy. The WHO released STOP TB Strategy in 2006 with six principal components to realize the global TB-related MDGs by 2015. These were pursuing high quality DOTS expansion and enhancement; Addressing TB/HIV, MDR-TB and other challenges; Contributing to health system strengthening; Engaging all care providers; Empowering patients and communities; and Enabling and promoting research.

India adopted the components of STOP TB Strategy and strived to achieve targets under it. National AIDS Control Programme (NACP) and RNTCP have developed “National framework of joint TB/HIV Collaborative activities” in 2007 which were revised in February 2008 to redefine the scope of TB/HIV collaborative activities being implemented in the country. Programmatic management of drug resistant (DR) TB services began in 2007 and national coverage has been achieved in March 2013. Scope of engagement of all care providers was expanded with revisions in schemes for involvement of private providers and NGOs in 2008 and Global Fund supported engagement of professional associations like Indian Medical Association (IMA) and Catholic Bishop Conference of India (CBCI). Task force mechanisms were established to engage medical colleges to support patient care, training, advocacy and research.

Emboldened by its achievements, the programme in 12th Five Year Plan (2012-17) has articulated National Strategic Plan with a vision of TB Free India. The goal of the NSP is to achieve universal access to quality TB diagnosis and treatment for all TB patients in the community. The objectives of the National Strategic Plan are

1. To achieve 90% notification rate for all cases
2. To achieve 90% success rate for all new and 85% for re-treatment cases
3. To significantly improve the successful outcomes of treatment of DR-TB Cases
4. To achieve decreased morbidity and mortality of HIV-associated TB
5. To improve outcomes of TB care in the private sector

To achieve these objectives, RNTCP further strengthened and improved the quality of basic DOTS services, align the sub-district level management unit with health system under National Health Mission [NHM], deploy improved rapid diagnostics to the field level, increase efforts to engage all care providers, strengthen urban TB Control, expand diagnosis and treatment of DR-TB, improving communication, outreach, and social mobilization and promoting research for development and implementation of improved tools and strategies. The Gazette of India, Ministry of Health and Family Welfare has notified for prohibiting the import of serodiagnostic test kits for TB and the manufacture, sale, distribution and use of such kits for TB, on 7th June 2012. A Government Order issued by the GOI in May 2012 mandates all healthcare providers to notify every TB case diagnosed and/or treated, to local authorities. To support TB notification and strengthen TB surveillance in general, a case based web based TB notification system – NIKSHAY was established to provide platform for notification from both public and private sector, decrease lead time of data transmission and increase use of information for programme management for betterment of care of delivery of services at local level.
RNTCP and World Health Organization jointly prepared Standards for TB Care in India (STCI) in 2014, which lays down uniform standards for TB care for all stakeholders in the country.

**Standards for TB Care in India (STCI)**

The vision of RNTCP is that the people suffering from TB receive the highest standards of care and support from all healthcare providers of their choice. It is spelt out in the National Strategic Plan (2012-17) to extend the umbrella of quality TB care and control to include those provided by the private sector.

The private sector holds a factual predominance of health care service delivery in India. There is very little information about TB patients from the private sector available to the programme and little is known about their quality of treatment, including treatment outcomes. The need for quality and standards for TB care is made particularly acute where a large unorganized private sector accounts for almost half of the TB care delivered in India.

Thus, it was felt essential to develop and disseminate the standards for TB care that is particularly relevant in Indian context, acceptable to the medical fraternity in both the public and private sector in India. Also, the availability of new diagnostic tools and strategies for early TB diagnosis, emerging evidences on existing regimens and newer regimens, and the need for better patient support strategies including addressing social inclusiveness necessitated the development of Standards for TB Care in India.

The standards in STCI differ from existing guidelines in that the standards present what should be done whereas guidelines describe how the action is to be accomplished. These standards represent the first what is expected from the Indian healthcare system. It is expected that the standards laid down in STCI are clear and usable and will be accessible to all TB providers as an easy reference.

Twenty six standards developed after a National Workshop with support from various public health administrators, programme managers, representatives from various professional associations (IMA, API, College of Physicians Association of India, IAP, FOGCI, etc.), academicians and specialists from public and private sectors (pulmonologists, physicians, surgeons, paediatricians, gynaecologists, orthopaedic surgeons, microbiologists, public health specialist etc.), donors, technical and implementation partners & pharmaceutical companies and pharmacists. There are six standards for diagnosis (standard 1 to 6), five for treatment (standard 7 to 11), nine for public health (standard 12 to 20) & six for social inclusion (standard 21 to 26).

The country achieved targets for TB under MDG and Stop TB Partnership. Post-MDG, the Global strategy & targets for prevention of TB care & control were endorsed by all member states at 2014 World Health Assembly. Achieving this global target is feasible only with the drastic decline in the TB deaths, cases & elimination of the catastrophic expenditures leading to elimination of economic & social burden of TB. To reach these ambitious goals, End TB strategy spells out the three pillars & components as in the table as below. Government of India is signatory to end TB strategy and is fully committed to implement its components under the programme.
END TB STRATEGY

VISION

A WORLD FREE OF TB
- Zero deaths, disease and suffering due to TB

GOAL

END THE GLOBAL TB EPIDEMIC

<table>
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<tr>
<th>INDICATORS</th>
<th>Milestones</th>
<th>Targets</th>
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<tbody>
<tr>
<td></td>
<td>2020</td>
<td>2035</td>
</tr>
<tr>
<td>Reduction in number of TB deaths compared with 2015 (%)</td>
<td>35%</td>
<td>75%</td>
</tr>
<tr>
<td>Reduction in TB incidence rate compared with 2015 (%)</td>
<td>20% (&lt;85/100,000)</td>
<td>50% (&lt;55/100,000)</td>
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<tr>
<td>TB-affected family facing catastrophic costs due to TB (%)</td>
<td>0</td>
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PRINCIPLES

1. Government stewardship and accountability, with monitoring and evaluation
2. Strong coalition with civil society organizations and communities
3. Protection and promotion of human rights, ethics and equity
4. Adaptation of strategy and targets at country level, with global collaboration

PILLARS AND COMPONENTS

1. INTEGRATED, PATIENT-CENTRED CARE AND PREVENTION
   A. Early diagnosis of tuberculosis including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
   B. Treatment of all people with tuberculosis including drug-resistant tuberculosis, and patient support
   C. Collaborative tuberculosis/HIV activities, and management of co-morbidities
   D. Preventive treatment of persons at high risk, and vaccination against tuberculosis

2. BOLD POLICIES AND SUPPORTIVE SYSTEMS
   A. Political commitment with adequate resources for tuberculosis care and prevention
   B. Engagement of communities, civil society organizations, and public and private care providers
   C. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
   D. Social protection, poverty alleviation and actions on other determinants of tuberculosis

3. INTENSIFIED RESEARCH AND INNOVATION
   A. Discovery, development and rapid uptake of new tools, interventions and strategies
   B. Research to optimize implementation and impact, and promote innovations
Health System structure & functions for delivery of TB care

Healthcare is one of India’s largest service sectors. Under the Indian Constitution, health is a state subject. Each state has its own healthcare delivery system in which both public and private (for profit as well as non-profit) actors operate.

Delivery of TB care in the public sector

The organisation at the national level consists of the Union Ministry of Health and Family welfare (MoHFW). In each State, the organisation is under the State Department of Health and Family Welfare that is headed by a State Minister and with a Secretariat under the charge of the Secretary/Commissioner (Health and Family Welfare).

a) In 2005, National Rural Health Mission (NRHM) was launched to provide accessible, affordable, accountable, effective and reliable primary health care facilities, to the rural population, especially vulnerable groups. In addition, the National Urban Health Mission (NUHM) was also launched to further strengthen urban health structure and both NUHM and NRHM have been clubbed together under National Health Mission (NHM) from 2013. The vision of NHM is “Attainment of Universal Access to Equitable, Affordable and Quality health care services, accountable and responsive to people’s needs, with effective inter-sectoral convergent action to address the wider social determinants of health”.

b) NHM further aims to provide support to the existing national programmes of health and family welfare including RCH-II, malaria, blindness control, iodine deficiency, filariasis, kala-azar, tuberculosis, and leprosy and for integrated disease surveillance

c) RNTCP is one of the components under the National Health Mission which is a flagship scheme under Govt. of India. The MoHFW follows equity-based approach to allocate funds under RNTCP to various States. The overall allocation is made on the basis of population of the states, disease burden and socio economic status. The financial management procedures for RNTCP are well established and administered by the Finance Cell of the CTD. These procedures are documented in manuals and guidelines available on the program’s website.

I. Institutional arrangements: Overall responsibility for financial management of the program is with the Central Tuberculosis Division (CTD), Directorate General of Health Services, Ministry of Health & Family Welfare (DGHS) a part of the National Health Mission of the MoHFW. At state level these are through state TB cell and at district level through district TB cell.

ii. Budget and release of funds: Program expenditures are budgeted in the Demand for Grants of the MoHFW under the Disease flexi-pool funding arrangement under two separate budget lines for Externally Aided Component (EAC) and General Component (GC).

iii. Fund flow: Fund flow for the program will remain within the existing financial management systems of MoHFW, which operates through the Centralized Pay and Accounts Office. Funds are being released to state in 2-3 instalments. All the states are required to submit the annual audit report to CTD by 30th September.
**RNTCP organogram**

RNTCP structure comprises of five levels: National, State, district, sub-district and peripheral health institution level.

**National Level**

Central TB Division (CTD) of Directorate General Health Services (DGHS) is the technical arm of the Ministry of Health and Family Welfare (MoHFW). CTD, under the guidance of DGHS, manages the National TB Control Programme for the entire country at the central level through a National Programme manager, Deputy Director General TB (DDG-TB). The financial and administrative control of the programme is managed by the Joint Secretary from the administrative arm of the MoHFW.

The CTD is supported by six national institutes: National Institute for Research in Tuberculosis (NIRT), Chennai, National Tuberculosis Institute (NTI), Bangalore, National Institute of Tuberculosis and Respiratory Diseases (NITRD), Delhi, National JALMA Institute, Agra, Regional Medical Research Centre, Bhubaneshwar and BMHRC, Bhopal, and National Task Force of Medical Colleges. Various committees of experts to guide the programme at different levels on technical & policy matters are there supporting Central TB Division.

**State Level**

The States have total ownership and accountability for the TB control in their state. State Health Society or its equivalent under National Health Mission of the state manages the TB Control Programme. A full-time State Tuberculosis Officer (STO), trained at national level and based at the State TB Cell (STC), is responsible for planning, training, supervising and monitoring the programme in all the districts of their respective states. STO is administratively accountable to the State Government, technically follows the instructions of the CTD, and coordinates with CTD and the districts and is assisted by other technical & secretarial staff.

State TB cell is being supported by State TB Training and Demonstration Centre (STDC) in many states through its three units – a training unit, supervision and monitoring unit and an Intermediate Reference Laboratory (IRL) supporting an effective Quality Assurance system of the Sputum smear microscopy network and lab services for PMDT (molecular DR testing and C&DST) in the State.

Each state also has one (1 for each 50 million population at least) fully operational State Drug Store (SDS). It is responsible for effective management of medicines and other logistics and ensuring uninterrupted supply of good quality 1\textsuperscript{st} & 2\textsuperscript{nd} line anti-TB medicines for adults and paediatric population.
**District Level**
The key level for the management of primary health care services is the district. The Chief District Health Officer (CDHO) / Chief District Medical Officer (CDMO) / Chief Medical Officer (CMO) / Civil Surgeon or an equivalent functionary in the district is responsible for all medical and public health activities including control of TB. The District Tuberculosis Centre (DTC) is the nodal point for TB control activities in the district. A full-time District Tuberculosis Officer (DTO), trained at national level & based at the DTC, is responsible for planning, training, supervising and monitoring the programme in the district. DTO is assisted by other technical & secretarial staff. The primary role of the DTC is managerial.

**Sub-District Level (Tuberculosis Unit Level)**
Integrating the TB control programme with the health system increases effectiveness and efficiency of TB care and control. India’s TB control programme has been mainstreamed efficiently with National Health Mission (NHM).

*A major organizational change in RNTCP is the creation of a sub-district level (Tuberculosis Unit - TU).* The TU is the nodal point for TB control activities in the sub-district. TUs are based mainly in NHM health blocks with the overall aim to align with NHM Block Programme Management Unit (BPMU) for optimum resource utilization and appropriate monitoring. In urban areas the TUs have been created based on a population of 1 per 2,00,000 (range 1.5 – 2.5 lakh). The Tuberculosis unit (TU) consists of a designated Medical Officer-Tuberculosis Control (MO-TC), as well as one full-time supervisory staff - Senior Treatment Supervisor (STS). One Senior TB Laboratory Supervisor (STLS) will continue to be in 5 lakh population and 1TBHV per one lakh urban population is there to support the urban TB control activities.

The Block Medical Officer also functions as a MO-TC who is trained in RNTCP at a state level institution. MO-TC has the overall responsibility of management of TB Control Programme at the TU and is expected to undertake supervisory visits for seven days in a month. The team of STS and STLS are under the administrative supervision of the MO-TC and the DTO. The TU will have one Microscopy Centre for every 100,000 population (50,000 in tribal, desert, remote and hilly regions) referred to as the Designated Microscopy Centre (DMC). Microscopy Centres are also located in Medical Colleges, Corporate hospitals, ESI, Railways, NGOs, private hospitals, etc.

**Peripheral Health Institutions (PHIs)**
For the purpose of RNTCP, a PHI is a health facility which is manned by at least a medical officer. At this level, there are dispensaries, PHCs, CHCs, referral hospitals, major hospitals, specialty clinics or hospitals (including other health facilities), TB hospitals, and Medical colleges within the respective district. All health facilities in the private and NGO sectors participating in RNTCP are also considered as PHIs by the programme. Some of these PHIs also function as DMCs. Peripheral health institutions undertake tuberculosis case-finding and treatment activities as a part of the general health services. In situations where more than one MO is posted in any of the peripheral health centres, one of them may be identified and entrusted with the responsibilities of the RNTCP.
TB Laboratory Services

The services of the laboratory are utilized for diagnosing TB & DR-TB cases and for monitoring of treatment of these patients. The Laboratory network under RNTCP is a 3-tier system for provision of diagnostic services and maintaining its quality.

A. The peripheral laboratories are situated in the public sector like the dispensaries, PHCs, CHCs, referral hospitals, major hospitals, specialty clinics, other sector hospitals, TB hospitals, Medical colleges and in the private/NGO sectors. For establishment of microscopy centre in a lab, it must have adequate physical infrastructure, Binocular microscope and a trained LT. These laboratories are covered under quality assurance mechanisms

   i. Some of the labs not having facility for sputum microscopy, function as a sputum collection centres, and such facilities are also established in areas such as the tribal, hilly, desert and difficult to reach areas of the country for improving the access to diagnostic services.

   ii. In addition, large hospitals and medical colleges have facilities of digital X-Ray, rapid molecular test (CBNAAT & LPA), FNAC, histo-pathology, and culture & DST for diagnostic services of TB.

B. At the state level a nodal laboratory is designated as intermediate reference laboratory (IRL) which is usually situated in the State TB Training and Demonstration Centre (STDC)/medical college/public health laboratory. The main functions of IRLs are monitoring of lab services across the state and maintenance of its quality through external quality assurance. There are 27 IRLs with facilities for culture & DST using Phenotypic (Solid – LJ & Liquid Culture – MGit) and Genotypic technology (LPA & CBNAAT).

C. At the central level there are six designated National Reference Laboratories (NRLs) namely National Institute for Research in Tuberculosis (NIRT), Chennai, National Tuberculosis Institute, Bangalore, National Institute of Tuberculosis and Respiratory Diseases (NITRD), Delhi, National JALMA Institute, Agra, Regional Medical Research Centre, Bhubaneswar and Bhopal Memorial Hospital & Research Centre (BMRHC), Bhopal. NIRT Chennai is also a Supra-Reference Lab (SRL) for World Health Organization (WHO) for the South East Asia Region, NTI is a WHO Collaborating Centre for Training, while NITRD is WHO centre of excellence in TB laboratory services. The NRLs are mainly responsible for External Quality Assurance of Lab network, drug resistance surveillance, training and research.
**Delivery of TB care services in the private sector**

The private sector referred to in this section is everything outside the ambit of the government run public health initiatives. The private sector in India varies widely in its size, nature of service delivery and the socio-economic groups served. It consists of a wide range of providers from individual medical practitioners of many different systems of medicine, including allopathic as well as Indian Systems of Medicine and Homeopathy, paramedics and even traditional healers who possess no formal training to private hospitals and nursing homes, NGO run hospitals, and corporate sector health care institutions.

The private sector holds a factual predominance of health care service delivery in India. As per National Sample Survey Organization report of 71st round of survey, more than 70% of patients seek care in private clinics or hospitals.

Delays in diagnosis, over-diagnosis of TB due to an over-dependence on X-rays, the use of multiple non-standard regimens for inappropriate durations, the lack of a mechanism to ensure the full course of treatment and to record treatment outcomes are some issues of concern in the private sector. Similar problems in varying degrees are encountered in other health sectors as well.

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<th>Advantages</th>
<th>Public Sector</th>
<th>Private Sector</th>
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<tr>
<td></td>
<td>Free diagnosis</td>
<td>Wide choices (&gt; 5 lac practitioners)</td>
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<td></td>
<td>Free treatment</td>
<td>Better access</td>
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<td></td>
<td>Standardized regimen</td>
<td>- Convenient timings</td>
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<tr>
<td></td>
<td>Referral and transfer system</td>
<td>- Shorter distances</td>
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<td></td>
<td>Supervision and monitoring</td>
<td>- Personal attention and care</td>
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<td></td>
<td>Accountability of treatment outcome</td>
<td>- Projected discounts</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Disadvantages</th>
<th>Public Sector</th>
<th>Private Sector</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Staff’s nonresponse to symptoms</td>
<td>Cost of clinical examination fees</td>
</tr>
<tr>
<td></td>
<td>Delays between tests and receiving results</td>
<td>Cost of diagnostic tests</td>
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<td></td>
<td>Difficulty in transporting specimens</td>
<td>Cost of drugs</td>
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<td></td>
<td>Financial expenditure on travel, food, daily necessities, extra medicines</td>
<td>Irrational prescriptions</td>
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<tr>
<td></td>
<td>Perceived low quality of services</td>
<td>Infrequent use of quality sputum tests for diagnosis of TB</td>
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The strategic vision of RNTCP is to lay down guidelines and norms for TB care in country. The underlying principle is for RNTCP to extend public services to privately managed patients. Standards for TB care in India, mandatory TB notification, NIKSHAY, ban on serodiagnostics and amendments in H1 schedule are among the tools to improve TB care services in private sector. Regulatory tools, however, are limited and partnership is preferred. Programme staff should understand that RNTCP needs private providers more than private providers need the RNTCP.
Other approaches include an expanded acceptance by RNTCP of internationally approved diagnostic and treatment protocols, reliance on market forces rather than normative exhortation, increased use of accreditation and contracting, further outreach to private laboratories, increased control of TB drugs, and innovative use of information and communication technologies for TB notification and treatment adherence monitoring. It is important to recognize that partnerships come in a wide variety of shapes and sizes, and operate at all levels, from local to global.

Model of care envisioned for delivery of services in continuum of care of TB patients from being a presumptive TB to the diagnosis, treatment and final treatment outcome in public and private sector is depicted below. It also shows what systems are in place for ensuring the various aspects of patient care in the public sector in the upper half and the other sectors in the lower half. All these systems ensure quality of services being provided to the patients irrespective of the place where the patient seeks care.

**Patients Centric Model of Care**
Case finding and Diagnosis strategy

To achieve universal access to early accurate diagnosis of TB and enhancing case finding efficiency, identification of presumptive TB cases at the first point of care and linking them to the best available diagnostic tests is of paramount importance. Early case detection is vital to interrupt the transmission of TB disease as highlighted in the 12th five year plan for TB control in India.

Early identification of people with a high probability of having active TB (presumptive TB) is the most important activity of the case finding strategy. Screening and diagnosing patients with appropriate tests and strategies will largely determine the response to appropriate treatment.

Patients attending health institutions - government/private need to be systematically screened for symptoms of TB by the health care provider. Presumptive TB patients should be promptly identified and are to be referred to diagnostic facility for appropriate investigation using the RNTCP request form for examination of biological specimen.

Passive case finding alone can lead to missed cases or delayed diagnosis. Enhanced outreach activities to detect more TB cases are critical to universal access. Screening for TB has also to be undertaken at every point of contact with health care among key population including clinically and socially vulnerable group of people.

Definitions of presumptive TB

2.1 Presumptive Pulmonary TB refers to a person with any of the symptoms and signs suggestive of TB including cough >2 weeks, fever > 2 weeks, significant weight loss, haemoptysis, any abnormality in chest radiograph.

Note: In addition, contacts of microbiologically confirmed TB Patients, PLHIV, diabetics, malnourished, cancer patients, patients on immune-suppressants or steroid should be regularly screened for sign and symptoms of TB

2.2 Presumptive Extra Pulmonary TB refers to the presence of organ specific symptoms and signs like swelling of lymph node, pain and swelling in joints, neck stiffness, disorientation, etc and/or constitutional symptoms like significant weight loss, persistent fever for ≥2 weeks, night sweats.

2.3 Presumptive paediatricTB refers to children with persistent fever and/or cough for more than 2 weeks, loss of weight*/no weight gain and/or history of contact with infectious TB cases**.

*History of unexplained weight loss or no weight gain in past 3 months; loss of weight is defined as loss of more than 5% body weight as compared to highest weight recorded in last 3 months.

** In a symptomatic child, contact with a person with any form of active TB with in last 2 years may be significant.

2.4 Presumptive DR TB refers to those TB patients who have failed treatment with first line drugs, paediatric TB non responders, TB patients who are contacts of DR-TB (or Rif resistance), TB patients who are found positive on any follow-up sputum smear examination during treatment with first line drugs, previously treated TB cases, TB patients with HIV co-infection.

DIAGNOSTIC TOOLS

Tools for microbiological confirmation of TB

All efforts should be undertaken for microbiologically confirming the diagnosis in presumptive TB patients. Under RNTCP, the acceptable methods for microbiological diagnosis of TB are:

Sputum Smear Microscopy (for AFB):
- Ziehl-Neelsen Staining
- Fluorescence staining
Culture:
- Solid (Lowenstein Jensen) media
- Automated Liquid culture systems e.g. BACTEC MGIT 960, BactiAlert or Versatrek etc.
- Drug Sensitivity Testing:
  - Modified PST for MGIT 960 system (for both first and second line drugs)
  - Economic variant of Proportion sensitivity testing (1%) using LJ medium (as a back up when indicated)

Rapid molecular diagnostic testing:
- Line Probe Assay for MTB complex and detection of RIF & INH resistance
- Nucleic Acid Amplification Test (NAAT) Xpert MTB/Rif testing using the GeneXpert system

Smear microscopy being the most commonly used method for microbiological diagnosis of TB for the last several decades, has had enormous value in TB diagnosis but with limited sensitivity, more so in children and PLHIV. Under RNTCP, two methods of microscopy are currently being used - ZN stain based microscopy using conventional microscope and Light Emitting Diode based Fluorescent Microscopy (LED FM).

Culture though highly sensitive and specific method for TB diagnosis, requires 2-8 weeks to yield results and hence alone does not help in early diagnosis. However culture will be used for follow up of patients on Drug Resistant TB treatment to detect early recurrence as part of using the indicator of relapse free cure.

Nucleic Acid Amplification Test (NAAT) provides accurate and rapid diagnosis of TB by detecting Mycobacterium tuberculosis (M. tuberculosis) and Rifampicin (Rif) resistance conferring mutations, in sputum specimen as well as specimen from extra-pulmonary sites. Presently, under RNTCP, its use is recommended for diagnosis of DR-TB in presumptive DR-TB patients and TB preferentially in key population such as children, PLHIV and Extra-pulmonary TB.

Other diagnostic tools

Radiography
Where available, CXR to be used as a screening tool to increase sensitivity of the diagnostic algorithm. Any abnormality in chest radiograph should further be evaluated for TB including microbiological confirmation. In the absence of microbiological confirmation, careful clinical assessment for TB diagnosis should be done. Diagnosis of TB based on X-ray will be termed as clinically diagnosed TB.

Tuberculin Skin Test (TST) & Interferon Gamma Release Assay (IGRA)
Standardized TST may be used as complementary test in children in combination with microbiological investigations, history of contact, radiology and symptoms. Interferon-Gamma Release Assays (IGRAs) are being used in place of skin test in low prevalence countries to detect TB infection. The exact advantage of IGRA in high burden countries like India is still not clear, hence these are not recommended for use for adults in diagnostic algorithm for tuberculosis in India.

Sero logical tests
The Government of India issued Gazette notification (vide 433E 7th June 2012) has banned the manufacture, importation, distribution and use of currently available commercial serological tests for diagnosing TB. These tests are not recommended for diagnosis of TB.
Process of Biological Specimen Collection & testing for microscopy
Medical Officers of healthcare facilities (governmental or non-governmental) should identify all presumptive TB from patients attending health facilities and refer them for examination using the RNTCP request form for examination of biological specimen. In Medical Colleges and other hospitals, indoor-patients suspected of TB should also be referred by the treating physician using the same RNTCP laboratory request forms.

Patients are given specimen containers with instructions to provide quality specimen which are then subjected for microscopy examination.

Two samples are collected within a day or two consecutive days. One sample is collected on the spot under supervision and other is collected early in the morning. The sputum containers should be labelled properly by writing the patient’s laboratory serial number on the side of the sputum container and not on the lid. Sputum should be at least 2 ml in quantity and preferably mucopurulent. Results of sputum tests should be reported within a day. If needed, storage of sputum samples should be in cool place/ refrigerator. A smear is made, fixed and stained using the Ziehl-Neelsen staining Fluorescence technique.

Transport of Biological specimens
Arrangements should be made locally for transporting the specimens to the DMC and for sending the results to the referring health centres. The specimens should be packed carefully in a box to avoid spillage. Before sending the sputum specimens to the DMC, the person should verify that:

1. The accompanying dispatch list contains the necessary information for all patients and clearly identifies the referring health facility collecting the sputum.
2. The total number of sputum specimens corresponds to the total number in the accompanying dispatch list.
3. The Specimen Identification Numbers on the sputum containers correspond to those on the accompanying list.
4. One RNTCP request form for examination of biological specimen is to be enclosed for each patient.
5. The health worker should then mark the date of dispatch on the dispatch list, put the list in an envelope and attach it to the box outside.
6. Sputum specimens should be examined by microscopy not later than 2 days after collection. Once examined, the microscopy results should be reported on the same day.
7. The containers along with the sample MUST be disinfected with 5% phenol solution and disposed as per guidelines after the sputum smears results are recorded in the laboratory Register.
8. Refer SOP for sputum collection & transportation (Annexure 3)

Smear preparation, Staining and Reading
Refer to SOPs of ZN Staining Techniques or Fluorescence Staining Techniques in (Annexure 1 & 2)

Diagnostic algorithm for pulmonary TB
All persons identified as presumptive TB patients in the health facility or those referred by other health care providers from the public / private health sector should be subjected to diagnostic tests as per the diagnostic algorithm(s).
**Diagnostic algorithm for pulmonary TB**

- **PLHIV**
  - **Presumptive TB patient**
    - **Smear Examination**
      - Smear Positive and CXR suggestive of TB
      - Smear Positive, but CXR not suggestive of TB
      - Smear Negative but CXR suggestive of TB
      - Smear Negative or Not Available & CXR not suggestive of TB or not available
        - **Clinical Suspicion High**
    - **CXR**
    - **CBNAAT**
      - MTB detected
        - Rif sensitive
          - Microbiologically Confirmed TB
          - Repeat CBNAAT on 2nd sample
        - Rif Indeterminate
        - Rif Resistant
          - Refer to management of Rif Resistance
      - MTB not detected or CBNAAT result not available
        - Consider alternate diagnosis and refer to specialist
        - Clinically Diagnosed TB
        - Alternate diagnosis

- **PMDT criteria, high MDR settings**
  - MTB detected
    - Rif sensitive
    - Rif Indeterminate
    - Rif Resistant
      - Refer to management of Rif Resistance
    - Repeat CBNAAT on 2nd sample
      - Indeterminate on 2nd sample, collect fresh sample for Liquid Culture / LPA

*All presumptive TB cases should be offered HIV counseling and testing; however diagnostic work up for TB must not be delayed.*
Note for diagnostic algorithm for pulmonary TB

A. All presumptive TB (specifically for PTB symptoms) will undergo sputum smear examination (ZN/LEDLM). Two specimens will be collected (spot-early morning or spot-spot). If the first smear is positive and the patient is not at risk for Drug Resistant (DR) TB, he will be categorized as microbiologically confirmed TB (sensitivity status not known).

B. Smear positive and presumptive MDR TB (as per PMDT guidelines) and in settings of high MDR TB (e.g., MDR TB rates >5% among new case and >20% among re-treatment cases), a CBNAAT will be performed to rule out rifampicin resistance before initiation of treatment where patients will be categorized as microbiologically confirmed Drug Sensitive (DST) TB or Rif resistant TB.

C. If the first smear is negative, CXR may be considered and if reported as suggestive of TB, the 2nd sample will be subjected to smear and CBNAAT simultaneously.

D. Based on CBNAAT results, patients will be categorized as microbiologically confirmed Drug sensitive TB or Rif resistant TB, if negative move to differential diagnosis for other etiology or point F.

E. A Rif indeterminate result will get an additional CBNAAT to get a valid result and in case of indeterminate on second occasion, an additional specimen will be collected and sent to the nearest Intermediate Reference Laboratory (IRL) or Culture & Drug Susceptibility Testing (C&DST) centre for LPA or Liquid Culture & DST as appropriate.

F. Wherever the facilities are available, efforts should be made to obtain DST results of all drugs by collecting additional samples and sending to nearest C&DST. (Subject to laboratory capacity).

G. If the both sputum smears and CXR are negative, and physician is still suspecting TB, he will refer patient to pulmonology expert/ chest specialist.

H. All key population (PLHIV, Children, EPTB, etc.) will preferentially get an upfront CBNAAT as per approved algorithm for PLHIV and TB HIV patients, pediatric TB and Extra pulmonary TB.

I. The algorithm does not mandatorily decide the “order to DO” the tests/ investigations. If needed/ available, appropriate tests may be done simultaneously but “order of consideration” for different types of test/ investigation results should be as per the algorithm. (e.g. If available, smear for AFB and CXR may be done simultaneously to avoid diagnostic delay/ patient’s day loss. But, smear results will be prioritized over CXR to make an early diagnosis). If patient walks in with the latest CXR, the same may be considered to reduce the diagnostic delay.

J. All diagnostic health care facilities should have TB labs that are quality assured by competent authority.

Diagnosis of Extra-pulmonary TB

Extra pulmonary tuberculosis (EPTB) refers to any microbiologically confirmed or clinically diagnosed case of TB involving organs other than the lungs such as lymph nodes, pleura, bones and joints, meninges of the brain, intestine, genitourinary tract, etc. A high level of suspicion of EPTB is important in patients with suggestive symptoms and signs.
All efforts should be made to establish microbiological confirmation in case of presumptive EPTB. Appropriate specimens from the presumed sites of involvement must be obtained from all presumptive EPTB patients for CBNAAT / Smear Microscopy / Culture & DST for \textit{M. tuberculosis} / histo-pathological examination, based on type of specimen and availability of facilities. CBNAAT is preferred over other tests. Chest X-ray, Ultrasonography, Computerised Tomography (CT) Scan, Magnetic resonance imaging (MRI) are other investigations which can be used as supporting tools for diagnosing EPTB.

Sensitivity of CBNAAT for TB diagnosis, when compared to liquid culture as a 'Gold Standard', is high in FNAC / biopsy specimen from lymph nodes, biopsy specimen from other tissues and cerebrospinal fluid (CSF), but lower in pericardial, ascitic and synovial fluid samples and still lower in pleural fluid. A positive CBNAAT result provides useful confirmation but a negative test does not always rule out TB, since the sensitivity of liquid culture itself in extra-pulmonary specimen is not very high. The laboratory SOP should be referred while using CBNAAT for extra-pulmonary samples. Tissues, to be tested by CBNAAT should be collected \textbf{without} formalin. Tissue samples should only be processed at laboratories with appropriate bio-safety requirements. \textbf{(Annexure 5)}

**Note on Diagnostic Algorithm for Extra Pulmonary TB**

1. CBNAAT in specimen from extra-pulmonary sites provides the following results:
   a. \textit{M. tuberculosis detected, Rifampicin sensitive}: Diagnosis of microbiologically confirmed EPTB is made.

   b. \textit{M. tuberculosis detected, Rifampicin indeterminate}: a repeat CBNAAT test is performed on the 2\textsuperscript{nd} specimen. If found to be indeterminate on the repeat test, an additional specimen should be collected and sent to the nearest RNTCP certified lab for culture and DST.

   c. \textit{M. tuberculosis detected, Rifampicin resistance}: patient should be treated as per PMDT guidelines;

   d. \textit{M. tuberculosis not detected}: The patient should be evaluated for TB based on clinical, radiological findings and other investigations like histo-pathological examination, ultra sonogram etc. In the event of a decision to treat with anti TB drugs, a diagnosis of clinically diagnosed TB can be made. Otherwise, an alternate diagnosis should be sought.

   e. Invalid test: a repeat CBNAAT test is performed on the 2\textsuperscript{nd} specimen, if available.

   f. Error/No result: a repeat CBNAAT test is performed on the same sample.

2. In case CBNAAT is not available, liquid culture needs to be performed. If culture is positive then diagnosis of microbiologically confirmed EPTB is made. Further work up may be done for all EPTB patients if they fall under the criteria of presumptive DR TB.

3. If investigations like CBNAAT/smear microscopy/culture turn out to be negative or if appropriate specimen is not available for these investigations, consultation with a specialist followed by other tests such as histo-pathology, radiology, cytology, biochemical examinations, etc., may be undertaken. In the event of a decision to treat with a full course of anti-TB drugs, diagnosis of clinically diagnosed EPTB is made.
Diagnostic Algorithm for Extra Pulmonary TB

Presumptive EPTB patient

Available

Appropriate specimen from site

If CBNAAT is not available

CBNAAT

MTB detected

Rif sensitive

Microbiologically Confirmed EPTB

Rif Indeterminate

Repeat CBNAAT on fresh specimen

Indeterminate on 2nd specimen, collect fresh sample for Liquid Culture

Rif Resistant

Refer to management of Rif resistance

MTB not detected.

Liquid Culture

Culture Positive

Microbiologically Confirmed EPTB

Culture Negative

No TB

Not Available

High Clinical suspicion

Use other diagnostic tools

Clinically Diagnosed TB

Alternate diagnosis

*If high clinical suspicion then follow high clinical suspicion flow diagram
Diagnosis of Paediatric TB

In children with presumptive paediatric TB, every attempt must be made to microbiologically prove diagnosis through examination of appropriate respiratory / non-respiratory specimens with quality assured diagnostic tests. Diagnosis of tuberculosis should not be made only on clinical features and further investigations are always necessary to establish the diagnosis.

In case of suspicion of pulmonary TB, sputum examination should be carried out among children who are able to give good quality specimens. CBNAAT is the preferred investigation of choice. If CBNAAT is not readily available or testing is not possible even by referral, smear microscopy should be performed. If *M. tuberculosis* is detected, by either of methods patient is diagnosed as microbiologically confirmed pulmonary TB. In situations where *M. tuberculosis* is not detected or specimen is not available, chest X-ray and Tuberculin skin test (TST) by Mantoux technique using 2 TU of PPD RT 23 should be done. For interpretation and further course of action, refer to the diagnostic algorithm for childhood pulmonary TB.

Notes on diagnostic algorithm
1. This algorithm is for children who are likely to have drug sensitive disease i.e. have not received ATT previously ever and are not presumptive drug resistant TB cases (lost to follow up, recurrent, treatment failure, HIV).
2. Proper Characterization of symptoms is very important starting point. Weight loss or not gaining weight should always be documented with appropriate and proper weighing.
3. Where CB NAAT is doable, smear examination may not be done. Whenever smear is used for diagnosis at least 2 samples should be sent while a single sample is subjected to CB NAAT. If a specimen is positive by any of these methods, the disease is labelled as Microbiologically confirmed TB.
4. Highly suggestive Chest X-ray refers to skiagrams showing either Miliary or lymphadenopathy (hilar or mediastinal) or chronic fibro-cavitatory shadows. If the radiological picture is highly suggestive of TB, then proceed to do further investigations irrespective of the TST result as the sensitivity of the test is not 100%.
5. Non Specific Chest X-ray: Refer to patterns other than highly suggestive like consolidations, in homogenous shadows or bronchopneumonia, etc.
6. Whenever indicated, alternative specimens (Gastric aspirate/ Induced sputum/ broncho-alveolar lavage) should be collected by a skilled health care provider, depending upon available infrastructure and sample should be subjected to CBNAAT.
7. Antibiotics like linezolid or any quinolone or Amoxicillin-Clavulanic acid should not be used as they have anti-TB action.
8. Children with persistent symptoms, non specific shadows and negative smears and negative other samples (G/A/S) by CB NAAT should be referred to experts for further work up of persistent pneumonia.
9. All TB cases diagnosed must be offered testing for HIV.
10. Instructions for administering PPD vials are placed at (Annexure 6)
11. Whenever RIF Resistant result is reported on CBNAAT further management should be carried out as per the guidelines on Drug Resistant TB

All presumptive DR TB patients should be appropriately followed up with PMDT guidelines. In case of suspicion of Extra Pulmonary TB, the diagnostic algorithm as given in section above may be followed.

There is no role for inaccurate / inconsistent diagnostics like serology (IgM, IgG, IgA antibodies against MTB antigens), various in-house or non-validated commercial PCR tests and BCG test. Currently there is no role of IGRAs in clinical practice for the diagnosis of TB.
Diagnostic algorithm for Pediatric Pulmonary TB

- Persistent Fever >2wk, without a known cause and/or
- Unremitting Cough for >2w and/or
- Wt loss of 5% in 3m or no wt gain in past 3 months

CBNAAT* (on sputum)

MTB not detected OR Sputum not available

MTB detected

Microbiologically confirmed TB Case

XRC highly suggestive

Gastric Aspirate/Induced Sputum for CBNAAT

+ve

-ve

No other likely alternative diagnosis Clinically Diagnosed TB case

X.Ray and TST

CXR NS shadows TST -ve

Give course of Antibiotics

Persistent shadow and symptoms

Gastric Aspirate/Induced Sputum for CBNAAT

+ve

-ve

Refer to expert for work up of persistent pneumonia

CXR Normal TST +ve

Evaluate for EPTB Refer to expert

CXR Normal TST -ve

Look for alternate cause

*If CBNAAT is not readily available, smear microscopy should be performed
Diagnosis of Drug Resistant TB

Drug resistant TB is a laboratory based diagnosis and is performed either by phenotypic Drug Susceptibility Testing using solid / liquid culture or genotypic testing for detection of resistance by Line Probe Assay / Cartridge Based Nucleic Acid Amplification Tests like Xpert MTB/Rif. CBNAAT detects resistance to only Rifampicin while LPA detects resistance to both Rifampicin and Isoniazid.

Genotypic testing is much faster than phenotypic methods, as these are not growth based tests. DST results by Solid LJ media has a turnaround time (TAT) of upto 84 days, Liquid Culture (MGIT) upto 42 days, LPA upto 72 hours and CBNAAT by 2 hours.

Under RNTCP, access to either CBNAAT or LPA is available and should be used for diagnosis of DR-TB. Refer to RNTCP Laboratory manual of Standard Operating Procedures for culture and DST, LPA and CBNAAT testing.

For CBNAAT, a single specimen is required for testing. The need for a second specimen for CBNAAT arises in case the result is “Invalid” or “Rif Indeterminate”. For “Errors”, “No Results” the test can be repeated on the same specimen after appropriate trouble shooting as per the user manual. Two specimens should be collected (spot-early morning or spot – spot) for examination by LPA which can be performed directly on sputum specimen which are positive on microscopy or on culture isolates of specimen which were negative on microscopy.

All efforts must be made to optimize the utilization of all locally available genotypic diagnostic capacity.

If Rifampicin Resistance is confirmed by CBNAAT or LPA, start Standardized Regimen for MDR TB and perform Liquid Culture DST at baseline to Levofloxacin and Kanamycin.

As guided by the diagnostic algorithm above, wherever the facilities are available, efforts should be made to obtain DST results of all the drugs intended to be used in regimen, by collecting additional samples and sending to nearest C&DST. (Subject to laboratory capacity which is dynamic and will be expanded in a phased manner). The programme has introduced Bedaquiline through conditional access programme initially at six sites with diagnostic protocol comprising of extended sets of DSTs. This diagnostic Algorithm for Bedaquiline containing and optimized background regimen is as follows

If Rifampicin Resistance is confirmed by CBNAAT or LPA, start Standardized Regimen for MDR TB and perform Liquid Culture DST at baseline to Levofloxacin, Moxifloxacin, Kanamycin, Capreomycin, Ethambutol, Ethionamide, Linezolid and Pyrazinamide along with LPA for Isoniazid on sample /culture isolate (reported as KatG or inhA mutation to decide on use of INH) with the next available specimen.

If resistance is detected to any second line injectable and/or fluoroquinolones, extended DST is performed for Para Amino Salicylic acid, Clofazamine and Bedaquiline (whenever available) and treatment modified accordingly.

If Rifampicin sensitive is detected by CBNAAT among presumptive DR-TB cases, send sample for LPA or liquid culture. All Isoniazid sensitive patients after testing with LPA or those while awaiting results of LPA should continue treatment with first line drugs as per RNTCP guidelines. If Isoniazid resistance is detected by LPA, report of result must also mention Kat G or INH-A mutation. Furthermore, Liquid Culture DST will be performed for Ethambutol, Pyrazinamide, Kanamycin, and Levofloxacin. If resistance is detected to second line injectable and/or fluoroquinolones, perform DST for remaining second line drugs as mentioned above. Initiate or modify treatment as per Drug susceptibility test results.
Diagnostic Algorithm for Bedaquiline containing and optimized treatment regimen

Presumptive TB Case

Key Population
PLHIV, Children, EPTB

Smear

Presumptive DR TB Case

Sm Negative

Sm Positive

Chest X Ray Abnormal* (Only for presumptive TB)

CBNAAT

RR or RH resistant

R & H sensitive

Only H resistant

LPA

Baseline LC DST to E, Z, Km, Cm, Lfx, Mfx (2.0), Lzd, Eto& LPA for H (In presumptive DR TB)
(In case of resistance to any FQ or SLID)
Perform extended DST for PAS, Cfx
BDQ DST (when available)

Continue treatment as per category in RNTCP guidelines

Baseline LC DST to E, Z, Km, Lfx
If resistance to FQ&/or SLID,
Perform extended DST (remaining SLD)

- If RR by CBNAAT, in addition to other drugs, H resistance (by LPA) to be done and treatment modified accordingly.
- For samples reported by LPA – report must mention H- resistance by Kat G or INH A mutation.
- For new patients (those who do not fit in the definition of presumptive DR-TB case diagnosed as TB with RR by CBNAAT – a second CBNAAT test will be offered along with liquid culture DST

* Those who do not fit in the definition of presumptive DR-TB case
Intensified TB Case Finding

Intensified case finding activity (ICF) is basically a provider initiated activity with the primary objective of detecting TB cases early by active case finding in targeted groups and to initiate treatment promptly. It can target people who anyway have sought health care with or without symptoms or signs of TB and also people who do not seek care. Increased coverage can be achieved by focusing on clinically, socially and occupationally vulnerable populations who have greater risk of TB. It must be remembered that 'Screening' is a dynamic process and the prioritization of vulnerable groups, choice of screening approach and screening interval should be regularly reassessed by the programme. Decisions on when and how to screen for TB, which vulnerable groups to prioritize and which screening tool to use will depend on the vulnerable group, the capacity of the health system, and the availability of resources.

Screening Tools

The most sensitive screening tool needs to be used to improve the pre-test probability of the subsequent diagnostic test and to reduce the number of people who need to undergo further diagnostic evaluation; and it may be different for different vulnerable groups or settings. Options for the screening tools include symptom screening and chest radiography. The following table shows the sensitivity and specificity of the screening tool options.

<table>
<thead>
<tr>
<th>Screening tests</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Screening</td>
<td>Cough &gt;= 2 weeks</td>
<td>56.2 (46.7, 65.4)</td>
</tr>
<tr>
<td></td>
<td>Any symptom</td>
<td>66.0 (56.3, 74.5)</td>
</tr>
<tr>
<td></td>
<td>Any symptom OR history of ATT</td>
<td>71.2 (64.8, 76.75)</td>
</tr>
<tr>
<td></td>
<td>CXR as initial screening tool</td>
<td>76.6 (70.8, 81.6)</td>
</tr>
<tr>
<td></td>
<td>Cough &gt;= 2 weeks OR CXR any abnormality</td>
<td>94.3 (91.1,96.4)</td>
</tr>
<tr>
<td>Secondary screening</td>
<td>CXR among those having Cough &gt;= 2 weeks</td>
<td>66.8 (60.5, 72.7)</td>
</tr>
<tr>
<td></td>
<td>CXR among those having any symptom</td>
<td>65.0 (58.8, 70.7)</td>
</tr>
<tr>
<td></td>
<td>CXR any abnormality among those having any symptom OR H/o ATT</td>
<td>67.1 (61.7-72.1)</td>
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</tbody>
</table>

Screening strategies

1. **Community screening** can be done by:
   Inviting people to attend screening at a mobile facility or a fixed facility. Invitations may target specifically people within a given vulnerable group, those
   • who have had recent close contact with someone who has TB and people with symptoms of TB
   • Going door to door to screen households
2. Institutional screening

- In Health care facilities: Systematically perform active screening of vulnerable individuals attending hospitals and other health care institution
- In congregate settings: Systematically perform active screening of vulnerable individuals in shelters, old age homes, refugee camps, correctional facilities and other specific locations such as workplaces.

Recommendations on Vulnerable groups to be screened

A vulnerable group is any group of people in which the prevalence or incidence of TB is significantly higher than in the general population. The recommended vulnerable groups to be considered for intensified case finding may be classified as follows:

<table>
<thead>
<tr>
<th>Clinical</th>
<th>Social</th>
<th>Geographical</th>
</tr>
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<tbody>
<tr>
<td>Clients attending HIV Care Settings</td>
<td>Prisoners</td>
<td>Urban Slums</td>
</tr>
<tr>
<td>Substance abuse including smokers</td>
<td>Occupations with risk of developing TB</td>
<td>Hard to reach areas</td>
</tr>
<tr>
<td>Co-morbidities like Diabetes Mellitus, Malignancies, patients on dialysis and on long term immunosuppressant therapy</td>
<td>People in Congregated settings – night shelters, De-addiction centres, Old age homes</td>
<td>Indigenous and tribal populations</td>
</tr>
<tr>
<td>Health Care Workers</td>
<td></td>
<td></td>
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<tr>
<td>Household &amp; Workplace Contacts</td>
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<td></td>
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<tr>
<td>Patients with Past History of TB</td>
<td></td>
<td></td>
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<tr>
<td>Malnourished</td>
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</tr>
<tr>
<td>Antenatal mothers attending antenatal clinics/MCH clinics</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For the groups classified above; the rationale of intensified case finding activities in the particular vulnerable group, the screening tool recommended and the strategy for screening are discussed in Annexure 7.

In all settings where intensified case finding is undertaken, systematic TB recording and reporting needs to include the following:

- A special register with individual-level information for each person screened may be used to obtain refined data about subcategories of persons within a vulnerable group.
- A register of all presumptive TB cases (Presumptive TB register) who undergo further diagnostic evaluation (if a register is used to collect individual-level information for all people who are screened, then this information can be included in it)
- A column in the laboratory registers for noting whether the tested patient was identified through screening, and to which risk group the patient belongs;
- A column in the treatment registers to note whether the patient was identified through screening, and to which risk group the patient belongs.
Adopting a well thought **ACSM** strategy and integrating it with the planning process for ICF will result in a multiplier effect in case finding efforts.

Utilizing Mobile Medical Units for screening presumptive TB patients in identified and hard to reach areas. Using Information, Communication & Technology (ICT) tools to enhance case finding are some the examples of innovation in ICF which can be adapted.

**Laboratory Quality Assurance**

**Quality Assurance (QA):** A System designed to continuously improve the reliability and efficiency of laboratory services. The Quality Assurance activities include:
- Internal Quality Control (IQC)
- External Quality Assurance (EQA)
- Quality Improvement (QI)

**For Sputum Microscopy**

The nationwide network of designated sputum smear microscopy laboratories provide appropriate and accessible quality assured TB diagnostic services. To meet the recommended standards of diagnostic practices for TB, the programme provides quality reagents and equipment to the laboratory network. A system has been designed for EQA of sputum smear microscopy and for supervision and monitoring of the diagnostic systems by the RNTCP which is carried out by Senior TB Laboratory Supervisor (STLS) locally and by the Intermediate (State level) and National Reference Laboratory at higher levels.

The NRLs work closely with the IRLs, monitor and supervise the IRL's activities and also undertake periodic training for the IRL staff in EQA, Culture & DST activities. Three microbiologists and four laboratory technicians have been provided by the RNTCP on a contractual basis to each NRL for supervision and monitoring of laboratory activities. The NRL microbiologist and laboratory supervisor/technician visit each assigned state at least once a year for 3 to 4 days as a part of on-site evaluation under the RNTCP EQA protocol.

The IRL ensures the proficiency of staff in performing smear microscopy activities by providing technical training to district and sub-district laboratory technicians and STLSs. The IRLs undertake on-site evaluation and panel testing to each district in the state, at least once a year.

Designated Microscopy Centre (DMC) is the most peripheral laboratory under the RNTCP network. For DMC and its supervisory staff, quality improvement trainings conducted periodically focus on issues such as human resources, trainings, AMC for binocular microscopes, quality specifications for ZN stains, RBRC blinding and coding issues, bio-medical waste disposal, infection control measures etc.

**Internal Quality Control (IQC):** of microscopy is a process of effective and systematic internal monitoring of the performance of bench work in the microscopy laboratory against established limits of acceptable test performance. This is accomplished by checking:

- a) Instruments: binocular/fluorescence microscopes, weighing machines, water baths etc.
- b) New lots of staining solutions.
- c) Smear preparation, staining, examination, grading, recording, reporting and storage.
- d) Appropriate disinfection and disposal.
**External Quality Assessment (EQA):** EQA is a process to assess laboratory performance which includes:

- On-site evaluation (unblinded reading of smears, QC and process of smear microscopy)
- Panel Testing (PT of lab personnel during OSE)
- Random blinded re-checking of routine smears

EQA also allows participant laboratories to assess their capabilities by comparing their results with those obtained in other laboratories in the network.

**Quality Improvement (QI):** A continuous process by which all components of smear microscopy are carefully analyzed for improving the diagnostic services. Data Collection, analysis and problem solving are the key components of this process.

The schematic representation of the EQA reporting process is shown below:

Quality assessment methods under RNTCP have been implemented for more than a decade now and it is therefore necessary to revise the modalities to the present day scenario as well as to have mechanisms to routinely monitor the quality parameters. Monitoring quality of sputum smear microscopy depends on the:

- Evaluation of entire process of smear microscopy.
- Quality of data collection, analysis and correct interpretation of the results.
- Identifying defects, followed by remedial action.
- Quality Improvement largely relies on effective on-site evaluations.

The mechanisms involved as well as appropriate data collection is revised periodically in consultation with the National Reference Laboratories. For further details refer to Guidelines for Quality Assurance of Smear Microscopy.
Quality Assurance for Culture and DST:

The components of quality assurance for Culture and DST include Internal Quality Control (IQC) and External Quality Assessment mechanisms.

Internal Quality control of LJ media is performed as a routine laboratory protocol and involves testing each batch of media for contamination as well as the use of control strain (H37RV) for growth parameters. IQC for MGIT is instrument guided. External quality assessment is not performed for culture.

Internal quality control of DST involves use of control strain (H37RV) as well as mono resistant strains (R mono and H mono) with every batch of DST performed.

External quality control for both LJ as well as MGIT is performed in two stages, initial retesting as one time activity where the NRL retests ten strains out of hundred performed by the participating laboratory. This is assessment of the laboratory in real time. As a second stage the participating laboratory is required to perform DST for thirty panel strains received annually from the NRL. This is the actual test of performance. For further details refer to Guidance for accreditation of laboratories under RNTCP for Mycobacterial Culture & DST.

Schematic representation of Proficiency Testing:

```
PROFICIENCY TESTING
Phenotypic methods

Retesting

100 DST results are reported by the IRL to the respective NRL

Of these, 10 are retested at NRL

Assessment of the laboratory performance in real time

Panel testing

30 cultures representing different resistant patterns are sent to the IRL by the NRL

DST is set up by the method routinely used by the laboratory

Actual test of performance
```
**Schematic representation of the process of Certification:**

RNTCP Certification process for TB culture and DST Laboratories

---

**Quality assurance for LPA:**
Initially, the NRL retests DNA extracts of twenty strains out of 50 performed in duplicates at the participating laboratory. This is followed by annual proficiency testing with panel strains.

**PT Benchmark:**
- Invalid LPA results – Less than 10%
- Contamination of negative control – Clean in all runs
- Internal Concordance – Greater than 95%
- External Concordance – Greater than 95%

**Quality assurance for CBNAAT:**
Each CBNAAT cartridge contains internal controls: Sample Processing Control (SPC) and Probe Check Control. If Probe Check fails, then the test is stopped, and an Error result is obtained. Troubleshooting is required based on the error code generated. Error rates higher than 5% should be investigated.

**SPC must be:**
- Positive when the result is **MTB Not Detected**.
- SPC can be negative or positive when the result is **MTB Detected**.
- The test result is **invalid** if the SPC is negative.

On site visits to CBNAAT sites should be planned at regular intervals to assess laboratory performance by district, state, IRL, NRL, CTD using the available standardized supervisory checklist for CBNAAT. CBNAAT sites in the districts should be visited by IRL/NRL during their EQA visits. Poorly performing sites should be prioritized for on-site visits.
Treatment of TB

Goal of TB Treatment

The goals of Tuberculosis treatment are:

- To decrease case fatality and morbidity by ensuring relapse free cure
- To minimize and prevent development of drug resistance
- To render patient non-infectious, break the chain of transmission and to decrease the pool of infection

Case definitions

I. Microbiologically confirmed TB case refers to a presumptive TB patient with biological specimen positive for acid fast bacilli, or positive for Mycobacterium tuberculosis on culture, or positive for tuberculosis through Quality Assured Rapid Diagnostic molecular test.

II. Clinically diagnosed TB case refers to a presumptive TB patient who is not microbiologically confirmed, but has been diagnosed with active TB by a clinician on the basis of X-ray abnormalities, histopathology or clinical signs with a decision to treat the patient with a full course of Anti-TB treatment.

In children, clinically diagnosed TB case is diagnosed based on the presence of abnormalities consistent with TB on radiography, a history of exposure to an infectious case, evidence of TB infection (positive TST) and clinical findings suggestive of TB in children in event of negative or unavailable microbiological results

Microbiologically confirmed or clinically diagnosed cases of TB are also classified according to:

- anatomical site of disease;
- history of previous treatment;
- drug resistance;

Classification based on anatomical site of disease

a) Pulmonary tuberculosis (PTB) refers to any microbiologically confirmed or clinically diagnosed case of TB involving the lung parenchyma or the tracheo-bronchial tree.

b) Extra Pulmonary tuberculosis (EPTB) refers to any microbiologically confirmed or clinically diagnosed case of TB involving organs other than the lungs such as pleura, lymph nodes, intestine, genitourinary tract, joint and bones, meninges of the brain etc.

*Miliary TB is classified as PTB because there are lesions in the lungs. A patient with both pulmonary and extrapulmonary TB should be classified as a case of PTB.*

Classification based on history of TB treatment

a) New case - A TB patient who has never had treatment for TB or has taken anti-TB drugs for less than one month is considered as a new case.

b) Previously treated patients have received 1 month or more of anti-TB drugs in the past.

   I. Recurrent TB case- A TB patient previously declared as successfully treated (cured/treatment completed) and is subsequently found to be microbiologically confirmed TB case is a recurrent TB case.

   II. Treatment After failure patients are those who have previously been treated for TB and whose treatment failed at the end of their most recent course of treatment.
III. **Treatment after loss to follow-up** A TB patient previously treated for TB for 1 month or more and was declared lost to follow-up in their most recent course of treatment and subsequently found microbiologically confirmed TB case

IV. **Other previously treated patients** are those who have previously been treated for TB but whose outcome after their most recent course of treatment is unknown or undocumented.

c) **Transferred In:** A TB patient who is received for treatment in a Tuberculosis Unit, after registered for treatment in another TB unit is considered as a case of transferred in.

**Classification based on drug resistance**

a. **Mono-resistance (MR):** A TB patient, whose biological specimen is resistant to one first-line anti-TB drug only.

b. **Poly-Drug Resistance (PDR):** A TB patient, whose biological specimen is resistant to more than one first-line anti-TB drug, other than both INH and Rifampicin.

c. **Multi Drug Resistance (MDR):** A TB patient, whose biological specimen is resistant to both isoniazid and rifampicin with or without resistance to other first line drugs, based on the results from a quality assured laboratory.

**Rifampicin Resistance (RR):** Resistance to rifampicin detected using phenotypic or genotypic methods, with or without resistance to other anti-TB drugs excluding INH. Patients, who have any Rifampicin resistance, should also be managed as if they are an MDR TB case.

d. **Extensive Drug Resistance (XDR):** A MDR TB case whose biological specimen is additionally resistant to a fluoroquinolone (ofloxacin, levofloxacin, or moxifloxacin) and a second-line injectable anti TB drug (kanamycin, amikacin, or capreomycin) from a quality assured laboratory.

**Drug regimen**

**Drug sensitive TB**

The RNTCP adopted thrice weekly regimen for treatment of drug sensitive TB until now. The programme is now introducing daily regimen for treatment of drug sensitive Tuberculosis among PLHIV and Pediatric TB patients in the entire country and for all TB patients in 104 districts initially. Rest of the country will follow intermittent regimen as per existing guidelines until the daily regimen in scaled up to the entire country. For detailed guidelines on intermittent treatment regimen for drugs sensitive TB, RNTCP training module 1-4 for programme managers may be referred to.

The principle of treatment for tuberculosis (other than confirmed Drug Resistant forms of TB) with daily regimen is to administer daily fixed dose combinations of first – line anti-tuberculosis drugs in appropriate weight bands.

For new TB cases, the treatment in intensive phase (IP) will consist of eight weeks of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol in daily dosages as per four weight band categories. There will be no need for extension of IP. Only Pyrazinamide will be stopped in the Continuation Phase (CP), while the other three drugs will be continued for another 16 weeks as daily dosages.

For previously treated cases of TB, the IP will be of 12 weeks, where injection Streptomycin will be stopped after 8-weeks and the remaining four drugs (INH, Rifampicin, Pyrazinamide and Ethambutol) in daily dosages as per weight bands will be continued for another 4-weeks. There will be no need for extension of IP. At the start of CP, Pyrazinamide will be stopped while the rest of the drugs – Rifampicin, INH and Ethambutol will be continued for another 20 weeks as daily dosages in the CP.
The CP in both new and previously treated cases may be extended by 12-24 weeks in certain forms of TB like CNS TB, Skeletal TB, Disseminated TB etc. based on clinical decision of the treating physician. Extension beyond 12 weeks should only be on recommendation of experts of the concerned field. Loose Drugs would be needed as substitutions in case of adverse drug reaction or with co-morbid conditions.

<table>
<thead>
<tr>
<th>Type of TB Case</th>
<th>Treatment regimen in IP</th>
<th>Treatment regimen CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>(2) HRZE</td>
<td>(4) HRE</td>
</tr>
<tr>
<td>Previously treated</td>
<td>(2) HRZES + (1) HRZE</td>
<td>(5) HRE</td>
</tr>
</tbody>
</table>

*Prefix to the drugs stands for number of months*

**MDR/RR-TB cases (without additional resistance)**

These patients are to be treated with standard treatment regimen for MDR-TB that contains 6 to 9 months of IP with Kanamycin, Levofloxacin, Ethambutol, Pyrazinamide, Ethionamide and Cycloserine and 18 months of CP with Levofloxacin, Ethambutol, Ethionamide and Cycloserine.

<table>
<thead>
<tr>
<th>Type of TB Case</th>
<th>Treatment regimen in IP</th>
<th>Treatment regimen CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin resistant + Isoniazid sensitive or unknown(^2)</td>
<td>(6-9) Km LfxEto Cs Z E H</td>
<td>(18)LfxEto Cs E H</td>
</tr>
<tr>
<td>MDR TB(^1)</td>
<td>(6-9) Km LfxEto Cs Z E (Modify treatment based on the level of INH resistance as per the footnote)</td>
<td>(18)LfxEto Cs E</td>
</tr>
</tbody>
</table>

All MDR-TB isolates would be subjected to LC DST at baseline for Kanamycin and Levofloxacin, the results of which would be received after 6-8 weeks. Appropriate modifications of the treatment regimens can be done in the presence of additional resistance.

**XDR TB**

XDR TB cases will be treated with the STR for XDR TB comprising of Injection Capreomycin, Moxifloxacin, Linezolid, PAS, Clofazimine High Dose INH & Co-Amoxyclova.

The duration of IP will be for 6-12 months. Only the injectables will be stopped in CP and the remaining medicines will continue for another 18 months in CP.

All DR-TB treatment regimen are to be given on daily basis under supervision.

<table>
<thead>
<tr>
<th>Type of TB Case</th>
<th>Treatment regimen in IP</th>
<th>Treatment regimen CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>XDR</td>
<td>(6-12) Cm, PAS, Mfx, High dose- H, Cfz, Lzd, Amx/Clv</td>
<td>(18) PAS, Mfx, High dose-H, Cfz, Lzd, Amx/Clv</td>
</tr>
</tbody>
</table>
Whenever DST pattern of extended panel of drugs would be available to guide the treatment like at six sites where Bedaquiline is introduced initially; the management protocol will follow essentially optimized regimen in case patients are diagnosed with drug resistance other than or in addition to MDR and XDR. Management of such patients is as follows.

**Mono/Poly Drug resistant TB**

On receiving the reports showing Mono/ Poly DRTB from the quality assured CDST laboratory, patients and their family members are counselled. Patient is referred for evaluation & initiation of the regimen for mono/ poly DR TB to the DR TB center. Repeat rifampicin DST is to be done in case, result of mono or poly drug resistant TB is available after 6-8 weeks.

The DR TB Center committee carries out the pre-treatment evaluation (including clinical and radiological evaluation) of the patient and initiates him/her on the treatment regimen.

- **Mono Drug Resistant TB**- The treatment regimen is consisting of Injectable SLD + FQ + Rifampicin + two out of the first line drugs (from H, E & Z) to which the patient is sensitive to make a total of 5 effective drugs regimen given daily.

- In case of **reported baseline additional resistance to other FLDs**, the regimen is Inj SLD + FQ + Rifampicin + any FLD to which patient is sensitive + one of the remaining Group 4 drugs (Ethionamide, Cycloserine, PAS).

*In addition, High Dose INH is added to the regimen if LPA shows inhA mutation or culture reports show low level INH resistance.*

The total duration of treatment will be 9 to 12 months. The Intensive Phase (IP) is for 3 months with scope for extension to a maximum of 6 months. The Continuation phase (CP) is for a fixed duration of 6 months. The patient is initiated on treatment at DR-TB Centre, and then sent back for ambulatory treatment to the DTO for continuation of treatment regimen and regular follow-up.

<table>
<thead>
<tr>
<th>Type of TB Case</th>
<th>Treatment regimen in IP</th>
<th>Treatment regimen CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin Sensitive INH</td>
<td>(3-6) Km Lfx R E Z</td>
<td>(6) Lfx R E Z</td>
</tr>
<tr>
<td>Resistant(^1) TB &amp; DST of SEZ not known</td>
<td><em>(modify treatment based on baseline DST report to E, Z, KM, CM, Lfx, Mfx)</em></td>
<td></td>
</tr>
</tbody>
</table>

In certain circumstances, the committee can decide to continue same treatment on which the patient was, if patient is clinically, radiologically & microbiologically better while recommending an extension in the duration of the regimen and more frequent sputum smear and/or cultures in follow-up.

After 6 to 8 weeks the CDST reports of the patient sent before the initiation of treatment becomes available. The DTO continues the treatment regimen if no additional drug resistance is detected on culture DST report. However, if the CDST report shows additional Drug resistance, the DTO once again performs Sputum smear and if the Sputum smear is positive, the patient must be once again tested for Rifampicin resistance by LPA/CBNAAT before referring the patient to DR TB Center for further evaluation.
**MDR/RR-TB cases with additional resistance**

In case of **additional drug resistance**, the treatment can be modified as follows:
- In case of resistance to Ethambutol, it is to be omitted.
- In case of resistance to Pyrazinamide, it is to be omitted.
- In case of resistance to both Ethambutol and PZA, PAS to be added in IP and CP
- In case of resistance to Levoﬂoxacin or Moxifloxacine, the sensitive one is to be used along with PAS and clofazimine.
- In case of resistance to both Levoﬂoxacin and Moxifloxacine, these drugs are to be replaced with Clofazimine, Linezolid and PAS in IP and CP. The duration of IP will be from 6 to 12 months.
- In case of resistance to any second line injectable (Kanamycin or Capreomycin), use one of the sensitive injectables.
- In case of resistance to all second line injectable, replace them with Clofazimine, Linezolid and PAS in IP and CP. The duration of IP will be from 6 to 12 months.

<table>
<thead>
<tr>
<th>Type of TB Case</th>
<th>Treatment regimen in IP</th>
<th>Treatment regimen CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDR or Rifampicin Resistant TB + Ethambutol resistance¹,²</td>
<td>(6-9) Km Lfx Eto Cs Z</td>
<td>(18) Lfx Eto Cs</td>
</tr>
<tr>
<td>MDR or Rifampicin Resistant TB + Pyrazinamide resistance¹,²</td>
<td>(6-9) Km Lfx Eto Cs E</td>
<td>(18) Lfx Eto Cs E</td>
</tr>
<tr>
<td>MDR or Rifampicin Resistant TB + Ethambutol + Pyrazinamide resistance¹,²</td>
<td>(6-9) Km Lfx Eto Cs PAS</td>
<td>(18)Lfx Eto Cs PAS</td>
</tr>
<tr>
<td>MDR or Rifampicin Resistant TB + Levoﬂoxacin</td>
<td>(6-9) Km Mfx Eto Cs Z E PAS Cfx</td>
<td>(18)Mfx Eto Cs E PAS Cfx</td>
</tr>
<tr>
<td>MDR or Rifampicin Resistant TB + Moxifloxacine</td>
<td>(6-9) Km Lfx Eto Cs Z E PAS Cfx</td>
<td>(18)Lfx Eto Cs E PAS Cfx</td>
</tr>
<tr>
<td>MDR or Rifampicin Resistant TB + Resistance to all Fluoroquinolones</td>
<td>(6-12) Km Eto Cs Z E PAS Cfx Lzd</td>
<td>(18) Eto Cs E PAS Cfx Lzd</td>
</tr>
<tr>
<td>MDR or Rifampicin Resistant TB + Resistance to Km only</td>
<td>(6-9) Cm Lfx Eto Cs Z E</td>
<td>(18)Lfx Eto Cs E</td>
</tr>
<tr>
<td>MDR or Rifampicin Resistant TB + Resistance to all SL Injectable</td>
<td>(6-12) Lfx Eto Cs Z E PAS Cfx Lzd</td>
<td>(18)Lvx Eto Cs E PAS Cfx Lzd</td>
</tr>
</tbody>
</table>
**MDR-TB with mixed patterns of resistance**

In MDR-TB cases with mixed patterns of resistance (any FLD/ Inj SLI/ FQ/ Ethionamide, PAS, LZ, CF), Standardised Treatment Regimen (STR) for MDR TB will be modified in the following way:-

<table>
<thead>
<tr>
<th>Type of TB Case</th>
<th>Treatment regimen in IP</th>
<th>Treatment regimen CP</th>
</tr>
</thead>
</table>
| Mixed resistance pattern (any FLD/ Inj SLI/ FQ/ Ethionamide, PAS, LZ, CF)³ | (6-9) Km LfxEto Cs Z E Modify based on resistance pattern: Use any SLI and FQ as per recommendation above. Consider other oral drugs as per DST pattern and Duration:  
  *If SLI & FQ are included:* Minimum 6 Drugs in IP.  
  *If SLI and/or FQ are not included:* Minimum 8-9 drugs are to be given in IP.  
  *In pre-XDR/XDR patients, duration of IP will be 6-12 months* | (18)LfxEto Cs Z E Duration:  
  If SLI & FQ are included: Minimum 4 Drugs in CP  
  If SLI and/or FQ are not included: Minimum 7-8 drugs in CP |

These regimen will be scaled up when DST guided treatment guidelines will be implemented for the entire country.

**Notes**
1. For Isoniazid resistance, decision on use of Isoniazid in the regimen depends on following:
   - If High level resistance detected by Liquid culture - omit INH.
   - If low level resistance detected by Liquid culture - add high dose INH.
   - If LPA reports INH resistance by Kat G mutation- Omit INH
   - If LPA reports INH resistance by INH A mutation- Use High dose INH. Ethionamide in the
     treatment regimen will be replaced with PAS

2. If RR by CBNAAT, add INH in the standard doses to the treatment regimen till results of LPA
   or Liquid culture DST are known.
   - For new patients diagnosed as TB and RR by CBNAAT, put up both a repeat CBNAAT &
     send sample for liquid culture. Till then - following will be the treatment:
     - If second CBNAAT also shows RR - start standard MDR-TB treatment regimen with
       INH till the results from culture DST are known. Perform DST to H & SLDST on the
       liquid culture.
     - If second CBNAAT shows R sensitive- Start regimen for new TB cases and wait for
       report of Liquid culture DST.
       - If Liquid culture shows R Sensitive - Continue regimen for new TB cases.
       - If Liquid culture shows R resistance-refer the patient to DR TB center
         committee for Clinical, Radiological & microbiological assessment and decision
         regarding starting standard MDR-TB treatment regimen or continuing regimen
         for new TB cases depending upon the response to treatment given so far.

3. For mixed resistance pattern, consider oral drugs in following sequence of preference
   - Pyrazinamide (If Sensitive), Ethambutol, Ethionamide, Cycloserine, Pas,
     Clofazimine,Linezolid, Co-Amoxycilav, High Dose INH& Clarithromycin

4. The regimen designing / modification will be the prerogative of the DR-TB centre
   committee only.

5. Surgery in M/XDR-TB patients:
   - All patients of M/XDR-TB should be evaluated for surgery at the initiation of treatment
     and/or during follow up.

Bedaquiline Conditional Access Programme: Introduction of new anti TB drug under RNTCP

Bedaquiline (BDQ): is a new class of drug, diarylquinoline that specifically targets mycobacterial
ATP synthase, an enzyme essential for the supply of energy to *Mycobacterium tuberculosis* and
most other mycobacteria. Strong bactericidal and sterilizing activities against *M. tuberculosis*
have been shown in pre-clinical, laboratory and animal experiments. The drug has a high volume
of distribution, with extensive tissue distribution, highly bound to plasma proteins and heptatically
metabolized. The drug has an extended half-life, which means that it is still present in the plasma
up to 5.5 months post stopping BDQ. The dosing schedule has been established after extensive
pharmacokinetic / pharmacodynamic (PK/PD) studies in animals and humans and hence needs
to be administered as per the manufacturer's advice. BDQ demonstrates no cross-resistance
with existing first- and second-line anti-TB drugs and has shown significant benefits in improving
the time to culture conversion in MDR-TB patients. In June 2013, WHO published interim policy
guidance for the use of BDQ in conjunction with the WHO-recommended MDR-TB treatments.
RNTCP is introducing BDQ through conditional access programme at 6 sites in the country
initially.

Criteria For Patients To Receive Bedaquiline

Basic criteria: The criteria for patients to receive BDQ as approved by the Apex Committee
is: adults aged ≥ 18 years having pulmonary MDR-TB.
Additional requirements
- Females should not be pregnant, or should be using effective non-hormone-based birth control methods. They should be willing to continue practicing birth control methods throughout the treatment period, or have been post-menopausal for the past 2 years.
- Patients with controlled stable arrhythmia can be considered after obtaining cardiac consultation.

Treatment with Bedaquiline Containing Regimen
Pre-treatment evaluation of patients
All eligible patients would be subjected to a thorough pre-treatment evaluation at the DR-TB centres as per the RNTCP PMDT Guidelines. In addition, some additional pre-treatment evaluations would be added for patients eligible for BDQ containing regimen:
Each of the DR-TB centres must ensure that the necessary laboratory capacity and consultancy services from various specialists are available in the sites, either in-house or through an outsourced mechanism supported under institutional/state govt. mechanisms.

Treatment initiation
While waiting for the results of baseline SLDST as detailed above, all patients diagnosed as MDR-TB/RR-TB using various technologies will be initiated on standard regimen for MDR-TB as per RNTCP PMDT Guidelines. Once the results of baseline SLDST are available, the patients eligible and consented to be treated with BDQ containing regimen will be identified and an appropriate regimen will be designed by the DR TB center committee.

All eligible patients need to be offered counseling along with a patient education booklet which will give details of the nature and duration of treatment including information on the new drug BDQ; need for regular treatment; possible side-effects of these drugs; drugs to be avoided with BDQ and the consequences of irregular treatment or premature termination of treatment. Female patients will receive special counselling on family planning. After this, a written informed consent will be obtained from patients before administration of BDQ containing regimen.

All patients would be counseled and managed indoor for a mandatory period of 2 weeks (14 days) to complete the initial 2 weeks of BDQ doses. The final decision of further duration of indoor management of the patients rests with the DR-TB Centre committee and must be well-documented for every patient. After discharge the treatment will be continued on ambulatory basis as per RNTCP PMDT guidelines with strict adherence of treatment and the follow up schedule.

All measures for airborne infection control must be implemented as per the national AIC guidelines while managing all TB patients.

The RNTCP PMDT treatment register has been updated. Once the BDQ CAP is initiated, this new format of the register will be used for all DR-TB patients by the concerned DR-TB centers. The patient would be registered in this updated register and all necessary records would be maintained as detailed in the guidelines.

Please refer to The Guidelines for use of Bedaquiline in RNTCP through conditional access under the Programmatic Management of Drug Resistant Tuberculosis (PMDT) in India for details of BDQ Conditional Access Programme.
**Drug Dosage**

**Drug Dosage for Adult TB**

<table>
<thead>
<tr>
<th>Weight category</th>
<th>Number of tablets (FDCs)</th>
<th>Inj. Streptomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensive phase</td>
<td>Continuation phase</td>
</tr>
<tr>
<td></td>
<td>HRZE</td>
<td>HRE</td>
</tr>
<tr>
<td>25-39 kg</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>40-54 kg</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>55-69 kg</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>&gt;=70</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

*Inj. Streptomycin to be added in IP phase for 2 months in the previously treated regimen of drug sensitive patients. In patients above 50 years of age, maximum dose of streptomycin should be 0.75gm.

Adults weighing less than 25 kg will be given loose drugs as per body weight. Dosages of loose drugs are given in appendix.

**Drug Dosage for Pediatric TB**

<table>
<thead>
<tr>
<th>Weight category</th>
<th>Number of tablets (dispersible FDCs)</th>
<th>Inj. Streptomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intensive phase</td>
<td>Continuation phase</td>
</tr>
<tr>
<td></td>
<td>HRZ</td>
<td>E</td>
</tr>
<tr>
<td>4-7 kg</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8-11 kg</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>12-15 kg</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>16-24 kg</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>25-29 kg</td>
<td>3 + 1A*</td>
<td>3</td>
</tr>
<tr>
<td>30-39 kg</td>
<td>2 + 2A*</td>
<td>2</td>
</tr>
</tbody>
</table>

*A=Adult FDC (HRZE = 75/150/400/275; HRE = 75/150/275)
## Dosage for DR-TB for adults

<table>
<thead>
<tr>
<th>S.No</th>
<th>Drugs</th>
<th>16-25 Kgs</th>
<th>26-45 Kgs</th>
<th>46-70 Kgs</th>
<th>&gt;70 Kgs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rifampicin*</td>
<td>300</td>
<td>450</td>
<td>600</td>
<td>600</td>
</tr>
<tr>
<td>2</td>
<td>Isoniazid§</td>
<td>200</td>
<td>200</td>
<td>300</td>
<td>450</td>
</tr>
<tr>
<td>3</td>
<td>Ethambutol</td>
<td>400 mg</td>
<td>800 mg</td>
<td>1200 mg</td>
<td>1600 mg</td>
</tr>
<tr>
<td>4</td>
<td>Pyrazinamide</td>
<td>500 mg</td>
<td>1250 mg</td>
<td>1500 mg</td>
<td>2000 mg</td>
</tr>
<tr>
<td>5</td>
<td>Kanamycin</td>
<td>500 mg</td>
<td>500 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>6</td>
<td>Levofoxacin</td>
<td>250 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>7</td>
<td>Ethionamide</td>
<td>375 mg</td>
<td>500 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>8</td>
<td>Cycloserine</td>
<td>250 mg</td>
<td>500 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>9</td>
<td>Na-PAS (80% weight/vol)^1</td>
<td>7.5 gm</td>
<td>10 gm</td>
<td>12 gm</td>
<td>16 gm</td>
</tr>
<tr>
<td>10</td>
<td>Pyridoxine</td>
<td>50 mg</td>
<td>100 mg</td>
<td>100 mg</td>
<td>100 mg</td>
</tr>
<tr>
<td>11</td>
<td>Moxifloxacin (Mfx)</td>
<td>200 mg</td>
<td>400 mg</td>
<td>400 mg</td>
<td>400 mg</td>
</tr>
<tr>
<td>12</td>
<td>Capreomycin (Cm)</td>
<td>500 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>13</td>
<td>Amikacin (Am)</td>
<td>500 mg</td>
<td>500 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>14</td>
<td>High dose INH (High dose-H)</td>
<td>400 mg</td>
<td>600 mg</td>
<td>900 mg</td>
<td>900 mg</td>
</tr>
<tr>
<td>15</td>
<td>Clofazimine (Cfz)</td>
<td>100 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
</tr>
<tr>
<td>16</td>
<td>Linezolid (Lzd)</td>
<td>300 mg</td>
<td>600 mg</td>
<td>600 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>17</td>
<td>Amoxyclav(Amx/Clv)(In child: WHO 80mg/Kg in 2 divided doses)</td>
<td>875/125 mg BD</td>
<td>875/125 mg BD</td>
<td>875/125 mg BD</td>
<td>875/125 mg BD</td>
</tr>
<tr>
<td>18</td>
<td>Clarithromycin (Clr)</td>
<td>250 mg BD</td>
<td>500 mg BD</td>
<td>500 mg BD</td>
<td>750 mg BD</td>
</tr>
</tbody>
</table>

*For mono-H resistant TB; ^1For Rifampicin Resistant TB

^1In case of PAS with 60% weight/volume the dose will be increased to 10 gm (16-25 Kg); 14 gm (26-45 Kg); 16 gm (46-70 Kg) and 22 gm (>70 Kg)
Dosage for MDR-TB in pediatric Patients (less than 30 kg body weight)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Doses*</th>
</tr>
</thead>
</table>
| Kanamycin / Capreomycin | 15-30 mg/kg  
                      | (SM 20-40 mg/kg)                   |
| Levo<5 yrs: 15-20 mg/kg split dose  
Levo>5 yrs: 10-15 mg/kg once day  
Moxi 7.5-10 mg/kg  |
| Ethionamide           | 15-20 mg/kg                       |
| Cycloserine           | 10-20 mg/kg                       |
| Ethambutol            | 15-25 mg/kg                       |
| Pyrazinamide          | 30-40 mg/kg                       |
| Na-PAS                | <30 kg: 200-300 mg/kg             |

Drug dosage for XDR TB paediatric patients

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Daily Dose*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inj. Capreomycin (Cm)</td>
<td>15-30 mg/kg</td>
</tr>
<tr>
<td>PAS</td>
<td>&lt;30 kg: 200-300 mg/kg</td>
</tr>
<tr>
<td>Moxifloxacin (Mfx)</td>
<td>7.5-10 mg/kg</td>
</tr>
<tr>
<td>High dose INH (High dose-H)</td>
<td>15-20 mg/kg#</td>
</tr>
<tr>
<td>Clofazimine (Cfz)</td>
<td>1 mg/kg (max. 200 mg / day) limited data</td>
</tr>
<tr>
<td>Linezolid (Lzd)</td>
<td>10 mg/kg TDS (max. 600mg /day) with pyridoxine</td>
</tr>
<tr>
<td>Amoxyclav(Amx/Clv)</td>
<td>80 mg/kg (based on amoxicillin component) in two divided doses (max,4gm amox + 0.5gm clav)</td>
</tr>
<tr>
<td>Clarithromycin (Clr)</td>
<td>7.5 mg/kg every 12 hours</td>
</tr>
</tbody>
</table>

* as per companion handbook to the WHO guidelines for the programmatic management of drug-resistant TB.

# Till the time data are available, adult dose is used

Operational guidelines for treatment initiation

By suspecting TB in a patient, the clinician assumes an important role of providing complete care to the patient including long-term relapse free cure from TB. S/he also assumes an important public health responsibility of preventing the transmission of disease. If the clinician is waiting passively for the patient to report with the result of diagnostic test, it may cause significant delay in initiation of treatment or the patient may be lost to follow up. Hence, clinicians who refer the presumptive TB/ drug resistant TB case for diagnosis are encouraged to actively trace the patients. Health facilities that diagnose patients who do not reside in their service delivery area have to refer the patient to the facility where the patient would undergo monitoring of treatment.

All TB patients are offered quality assured anti-TB drugs under RNTCP. Treatment should be initiated by a trained medical officer. In most of the situations, treatment process may be initiated in the peripheral health institution which caters to the patient's residential area. In special circumstances, patients may have to be initiated on treatment in institutions outside their residential areas. eg. patient admitted in medical college hospital.
The information required for treatment initiation of TB patients are drug sensitivity pattern and history of anti-TB treatment. Based on it, decision on treatment to be taken as follows:

<table>
<thead>
<tr>
<th>History of treatment</th>
<th>Drug sensitivity status</th>
<th>Type of regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>Drug sensitive or DST unknown / awaited</td>
<td>Regimen for new case</td>
</tr>
<tr>
<td>Previously treated</td>
<td>Drug sensitive or DST unknown* / awaited</td>
<td>Regimen for previously treated case</td>
</tr>
<tr>
<td>New or previously treated</td>
<td>Drug resistant</td>
<td>Regimen based on DST pattern</td>
</tr>
</tbody>
</table>

*If DST is unknown, the patient should be offered DST based on current criteria of presumptive DR-TB patient. Four sets of drug sensitivity patterns may be offered based on availability of DST services.

- Rifampicin alone, where a CBNAAT is used for diagnosis.
- Isoniazid and Rifampicin where a LPA is used for diagnosis.
- A detailed first line pattern with Isoniazid, Rifampicin, Ethambutol and Streptomycin if a first line liquid DST is used.
- A second line DST pattern for second line drugs as may be available

The medical officer should record the weight of the patient. It is ideal to record the height also, to assess the Body Mass Index (BMI), which would provide a good indicator for prognosis of the disease. The patients should be given dosages depending on body weight in weight bands.

The medical officer of peripheral health facility can initiate treatment based on abovementioned information. However, all DR-TB patients should be treated with active involvement of DR-TB centre.

A proper pre-treatment evaluation is essential for each DR-TB patients (Rifampicin resistant / mono-/poly- resistant TB / MDR / XDR. For pre-treatment evaluation, a patient needs to be referred to appropriate health facilities where clinical competency to carry out such assessment is available. The pre-treatment evaluation includes a thorough clinical evaluation by a physician, chest radiograph, and relevant haematological and bio-chemical tests detailed in the box below.

**Pre-treatment evaluation for DR-TB patients**
1. Detailed history (including screening for mental illness, seizer disorder, drug/alcohol abuse etc.)
2. Weight
3. Height
4. Complete Blood Count with platelets count
5. Blood sugar to screen for Diabetes Mellitus
6. Liver Function Tests
7. Blood Urea and S. Creatinine to assess the Kidney function
8. TSH levels to assess the thyroid function (TSH levels alone are usually sufficient to assess the thyroid function of the patient)
9. Urine examination – Routine and Microscopic
10. Pregnancy test (for all women in the child bearing age group)
11. Chest X-Ray
12. ECG (if Moxifloxacin is to be used)
13. Serum electrolytes (if Capreomycin is to be used)
• All DR-TB cases will be offered referral for HIV counselling and testing at the nearest centre if the HIV status is not known or the HIV test is found negative with results more than 6 months old. If patient is HIV positive refer her/him to ART centre (if not on ART)
• Surgical evaluation should be added to the pre-treatment evaluation wherever indicated
• Preferably, pre-treatment evaluation should be carried out at DR-TB centre where DR-TB committee with group of experts are available. In this case, the patient should be referred to the DR TB center for admission & initiation of treatment with their DST result and referral for treatment form. Alternatively, district TB Officer can arrange pre-treatment evaluation at district level linked DR-TB centre or even at sub-district level health facility, in case the patient is unable to get hospitalized and to avoid any delay in initiation of treatment. In such case, the results of pre-treatment evaluation are communicated to DR-TB Centre Committee and on approval; the regimen for DR-TB can be initiated at the DTC.

Patient Flow in case of TB patients
• Before initiating the treatment, all the TB patients should be counselled thoroughly. It is advisable to involve close family members during the counselling, since family support is an essential component in the management.
• Educate the patient and family members about the disease (type of disease and mode of spread) and the treatment (dosage schedule, duration, common side-effects and methods to prevent them).
• Counsel the patient and family members to ensure treatment adherence (importance of need for regular treatment and consequences of irregular treatment or premature cessation of treatment, monitoring of progress until completion of treatment).
• Explain patients on prevention of transmission of disease (cover cough, proper disposal of sputum) and encourage him to get all his close contacts (especially household contacts) screened at the earliest.
• It is important to look for co-morbidities like diabetes, liver or renal diseases, neurological disorders etc. It is also important to look for substance abuse especially tobacco (in any form) & alcohol. Socioeconomic status of the patient may be assessed to link him/her with appropriate treatment support schemes.
• Medical Officer needs to open a treatment card (in duplicate when required) for each patient at the time of initiation of treatment. Each patient must be given TB Identity Card.
• Drugs should be made available at the treatment centre along with the TB treatment Card. Appropriate treatment adherence and monitoring mechanisms should be planned by the MO at the time of treatment initiation in consultation with the patient and the peripheral health worker who is responsible for monitoring treatment adherence.
• Assure the patient that s/he will be supported during the entire course of treatment by the MO and peripheral health care workers.
• Medical officer should make efforts to get HIV testing done in all cases of TB. This is important to ensure all HIV positive TB patients receive ART and CPT. Ideally all presumptive TB patients have to undergo HIV screening. If not, offer HIV screening. All HIV positive TB patients have to be referred to ART centre for initiation of ART and CPT.
Patient Flow in case of DR-TB patients

- DR-TB Centre should be involved actively in management of all DR-TB patients.

- DR-TB Centre will be the reporting unit for catering districts and will register all DR-TB cases of respective districts in DR-TB treatment registered with issue of unique DR-TB number.

- Treatment card of DR-TB patients admitted at DR-TB centre for pre-treatment evaluation will be opened by Medical Officer of DR-TB Centre.

- In case, a patient is not evaluated at DR-TB centre, results of the pre-treatment evaluation will be communicated to the DR-TB Centre committee for a decision to initiate the patient on treatment.
  - On receiving an affirmation from the DR-TB Centre committee the DTO will open the treatment card and start the patient on treatment.
  - A copy of the treatment card will be sent to the DR-TB Centre for their record and registration in the PMDT register.
  - On registration the DR-TB Centre will inform the PMDT TB number to the DTO.

- After pre-treatment evaluation and initiation of treatment, the patient should be referred back to the residence district / PHI with up to a maximum of one week’s supply of drugs, arrangements for injections in transit, and a copy of the treatment card and referral form.

- The respective DTO / MO-PHI should be informed by the MO DR-TB centre / DTO on referral of patients for ambulatory care in advance, by means of the RNTCP PMDT referral for treatment form via email.

- Drugs provided to the patients to cover for transit period may be counted as unsupervised doses. However, as far as possible efforts should be made by the district staff to restrict these transit doses.

- The DTO arranges for availability of the monthly IP drug box (from the TU) and the patient records at the identified treatment support Centre with information to the respective MO-PHI.

- This MO-PHI is responsible for supplying the treatment records and the drugs to the designated Treatment supporter. The MO-PHI will need to make suitable arrangements during the intensive phase of the treatment for daily injections including free needles and syringes.

- The overall responsibility of the patient on treatment including follow up is with the MO-PHI from where the patient is taking the treatment.
**Treatment support program**

Adherence to regular and complete treatment is the key to relapse free cure from TB. To assess and foster adherence, a patient-centred approach to administration of drug treatment, based on the patient's needs and mutual respect between the patient and the provider, should be developed for all patients.

A good treatment support plan should be developed at the time of initiation of treatment. This plan should include initial and frequent follow-up counselling of the patient and family members, supervision of treatment by a trained treatment supporter (a health worker or community volunteer), locally managed additional nutritional support, retrieval of treatment interrupters, screening for adverse reactions, psycho-social support, co-morbidity management and follow up laboratory investigations.

Direct observation of treatment is one of the best practices to promote adherence. It ensures that the patient consumes every dose of the treatment before a trained health worker and provides additional opportunity to support treatment. **However, the principle of direct observation is to be applied logically and judiciously.**

A treatment supporter who is acceptable, accessible to the patient and accountable to the health system should be identified and trained. A health worker in the hospital/health centre may be the best person to provide all the envisaged components of treatment support program. However, access to such a health worker in person, place and time may be limited since the centre may be far away from patient's residence, working hours may be restricted and the worker may be away on field visits. Compelling the patient to travel long distance to avail directly observed treatment is against the principles of patient centric approach. Hence all efforts must be put in to find a treatment supporter close to the patient's residence. Accumulating evidence has pointed to the effectiveness of a wide variety of approaches including community and family-centered DOT, which is more achievable for most developing healthcare systems and produce comparable outcomes to DOT by healthcare worker.

Wherever appropriate, a family member can also be assigned with the responsibility of observing treatment. Such situations may arise with sick and bed ridden patients, children, long-day workers etc. In such situations, the family member who is assigned with the responsibility to observe treatment should be trained well and supported during the process by a health worker by frequent visits to the house.

Each patient and his/her treatment supporter should be supervised by a health worker. It may be a peripheral health worker in the public health system. If the patient is initiated on treatment by a private health care provider, public health system may offer this supportive role when requested.

While observing treatment is one of the best modalities of promoting treatment, other modalities also may be deployed to further enhance adherence to treatment. Intelligent deployment of information communication technologies (ICT) is an example of such modalities. A patient who is unable to undergo supervised treatment should not be denied treatment. Frequent on-job travellers, truck drivers, sailors etc may require identification of proper treatment supporter. To promote treatment adherence among these patients, ICT modalities like frequent calls, SMS reminders, IVRS etc. may be deployed. [Box: Choices for ICT based Treatment adherence support]

Patient may require mobility support if s/he prefers observation of treatment outside his residence. Counselling may be required to quit substance abuse. Nutritional assessment & support, ancillary drugs, co-morbidity management, compensation for lost wages etc. are some other requirements.
To avail these, Healthcare providers should endeavor to derive synergies between various social welfare support systems like RSBY, TB pension schemes, national rural employment guarantee scheme, corporate social responsibility (CSR) initiatives, counselling centres etc., to mitigate out of pocket expenses such as transport and wage loss incurred by people affected by TB.

All individuals with active TB should receive (i) an assessment of their nutritional status and (ii) appropriate counselling based on their nutritional status at diagnosis and throughout their treatment. (iii) If malnutrition is identified, it should be managed according to WHO recommendations. Linkages for extra nutritional support for TB patients or of his/her contacts on IPT may be explored with existing Govt. schemes like public distribution system (PDS) or Food security act.

Under the programme, compensation is provided for transport costs incurred by DR TB patient for sending specimen for follow up or for travel to DR-TB centre. In addition, TB patients in tribal and difficult areas get Rs. 750. Treatment supporters are also provided incentive to ensure completion of treatment as below:

<table>
<thead>
<tr>
<th>Category</th>
<th>Compensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category I</td>
<td>Rs. 1000 per patient</td>
</tr>
<tr>
<td>Category II</td>
<td>Rs. 1500 per patient</td>
</tr>
<tr>
<td>Category IV / V</td>
<td>Rs. 5000 per patient</td>
</tr>
</tbody>
</table>

The compensation may be given to TB HIV patients for visits to ART centers. For enablers or incentives refer to Annexure 8. If required, linkages with various social support systems to be explored and ensured, for additional treatment support. Capacity building and engaging with local community based organizations, self-help groups, patient support groups, PRI could prove to be effective intervention to promote treatment adherence.

All patients should have free or affordable quality assured diagnostic and treatment services, which should be provided at locations and times so as to minimize workday or school disruptions and maximize access.
**Box: Choices for ICT based Treatment adherence support**

**Mobile based “Pill-in-Hand” adherence monitoring tool** In this mechanism, each time a patient takes a dose of medication, a hidden number appears which is printed on the strip behind the drug. The patient need to send a missed call to a particular contact number with the digits appeared on drug package. This will be documented at a centralized ICT unit. And thus, an electronic treatment record of each patient will be maintained to monitor the treatment adherence.

Because the sequence of hidden numbers cannot be predicted by patients, but are known by the system for each month of medication prescribed, the system offers high confidence that patients who respond correctly have indeed dispensed their medication.

S/he can also be providing the option of where in the patients treatment would be remotely followed up with help of Interactive Voice Response (IVR), SMS reminders.

Specially designed **electronic pill boxes** or strips with GSM connection and pressure sensor can be used to monitor the pill consumption by tracking the weight of the remaining pills.

The treatment provider can use the **Patient Compliance toolkit**; a mobile app for patients to report treatment compliance using video, audio or text message.

**Automated pill loading system**, which will load the dosage as per the pre-programmed settings. Medication dispenser: a color-coded reminder system built in the dispenser that will hold drugs.

Treating doctors can be provided with **innovatively designed cards** to educate them on correct TB prescription methods. Doctors will then give these cards to TB patients, instructing them to SMS the server/ customer care centre (CCC) the unique code on the card which will register them on the network and also SMS the unique codes printed on their TB drugs as they take them. The CCC will then deliver phone interventions like reminders to take medicines, financial incentives, follow up calls, and TB health tips via SMS and phone balance recharge, mobile APP for scheduled dose reminders and alerts.

A **Short Messaging service (SMS) gateway** to be made available by which the patient can report day to day events like pill consumption, minor side effects or his need for help through simple and shortcut SMS templates. The gateway can allow incoming services in pre-recorded or Interactive Voice Response (IVR) mode to inform patients about their test results, as follow up reminders and as periodic counselling messages.
Follow up of Treatment

Patients should be closely monitored for treatment progress and disease response. There are two components of follow up: (1) Clinical follow up and (2) Laboratory follow up

1. **Clinical follow up** should be done at least monthly. Patient may visit the clinical facility for reviews or the medical officer may conduct the review when he visits the house of the patient. Improvement on chest symptoms, increase in weight etc. may indicate good prognosis. Control of co-morbid conditions like HIV and diabetes by appropriate treatment is essential for getting a better prognosis to TB treatment. Symptoms and signs of adverse reactions to drugs should be specifically asked. Detailed description of symptoms and signs of adverse reaction to anti-TB drugs and pharmacovigilance program is described in relevant section.

2. **Laboratory investigations** may be those to assess the prognosis of the disease or to manage co-morbidities or adverse reaction. In case of pulmonary tuberculosis, sputum smear microscopy should be done at the end of IP and end of treatment. A negative sputum smear microscopy result at the end of IP may indicate good prognosis. However, in the presence of clinical deterioration, the medical officer may consider repeating sputum smear microscopy even during CP. This will provide the patient an early opportunity to undergo drug susceptibility testing if s/he is found to be sputum smear positive. At completion of treatment, a sputum smear and/or culture should be done for every patient. This is very important because, culture is a more sensitive and specific test compared with smear microscopy to detect the presence of M.tb in biological specimens.

   Chest x-ray may be a good tool to assess the progress and it is to be offered to drug sensitive pulmonary TB patients whenever required and available. For drug resistant TB patients, it is to be carried out at end of IP, at end of treatment and whenever required.

   Response to treatment in extrapulmonary TB may be best assessed clinically. Help of radiological and other relevant investigations may be taken.

   **Response to treatment in children:** In children in their early ages are unable to produce sputum, the response to treatment among them may be assessed clinically. The help of radiological and other relevant investigations may also be taken.

   **Long term follow up:** After completion of treatment, the patients should be followed up at the end of 6, 12, 18 & 24 months. In presence of any clinical symptoms and/or cough, sputum microscopy and/or culture should be considered. This is important in detecting recurrence of TB at the earliest.

   **In case of DR-TB patients,** the DTO will ensure that an updated copy of the treatment card is sent to the designated DR-TB Centre, preferably electronically, every month for updating the DR-TB Register. Clinical follow-up should be done monthly. For collection of the follow-up samples for culture, the patient will need to go to their respective sputum collection centre, where the DTO will arrange for the samples to be collected and transported to the respective RNTCP-certified Culture and DST laboratory. The patient will need to go to the DR-TB Centre for the decision to end treatment, for managing severe adverse drug reactions, and for any change of regimen or dosage. All referrals from the DTC to the DR-TB Centre or vice versa should be made on Referral for Treatment Form. The receiving health facility should communicate the receipt of patient to the referring centre through an e-mail.
<table>
<thead>
<tr>
<th>Type of Case</th>
<th>Follow up schedule</th>
<th>Extension of treatment</th>
<th>Action on follow up positive</th>
<th>Long term follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug sensitive Pulmonary TB (New &amp; Previously treated TB)</td>
<td><strong>Microbiological</strong>: One specimen at the time of completion of the intensive phase of treatment, and at the end of treatment. <strong>Weight</strong>: Monthly <strong>Chest X-Ray</strong>: if required <strong>Physician evaluation</strong>: whenever required</td>
<td>Extension of IP is not required</td>
<td>If the sputum smear is positive in follow-up at any time during treatment, DST should be done as per presumptive DR-TB case</td>
<td>After completion of treatment the patients should be followed up with clinical and/or sputum examination at the end of 6, 12, 18 and 24 months.</td>
</tr>
<tr>
<td>Multi Drug resistant Pulmonary TB (with or without additional drug resistance)</td>
<td><strong>Microbiological</strong>: One sputum specimen will be collected and examined by culture at least 30 days apart from the 3rd to 7th month of treatment (i.e. at the end of the months 3, 4, 5, 6 and 7) and at 3-monthly intervals from the 9th month onwards till the completion of treatment (i.e. at the end of the months 9, 12, 15, 18, 21 and 24). If any culture during CP or end of treatment is positive then it should be followed by monthly culture for 3 months. <strong>Weight</strong>: Monthly <strong>Chest X-Ray</strong> at end of IP, end of treatment and whenever clinically indicated <strong>Physician evaluation</strong> including adverse drug reaction monitoring every month for six months, then every three months for two years <strong>S. Creatinine</strong> monthly for first 3 months,</td>
<td>In MDR TB cases IP can be extended for maximum three months (maximum duration of IP – 9 months). In all MDR TB with additional drug resistant cases (including XDR TB) patients, IP can be extended for maximum 6 months (maximum duration of IP – 12 months)*.</td>
<td>On follow up if sputum culture is found to be positive at 6 months or later, repeat DST for second-line drugs to decide on further course of action. DST to other additional second line drugs may also be done if laboratory facilities are available to guide treatment.</td>
<td></td>
</tr>
</tbody>
</table>
then every 3 months during the injectable phase
**Thyroid Function Test** during pre-treatment evaluation and whenever indicated
**For additional drug resistance :-**
ECG: once a month in IP whenever Moxifloxacin is used
**Complete Blood Count with Platelets Count:** weekly in first month, then monthly to rule out bone marrow suppression and anaemia as a side effect of Linezolid
**Kidney Function Test**- monthly creatinine and addition of monthly serum electrolytes to the monthly creatinine during the period that Inj. Capreomycin is being administered
**Liver Function Tests:** monthly in IP and 3 monthly during CP
**Chest X-Ray:** every 6 months in XDR-TB patients

| Mono- / Poly-Drug resistant Pulmonary TB | Microbiological: One sputum specimen is collected and examined with smear and culture at 2nd and 3rd months & then culture examination at 3-monthly intervals till completion of the treatment. **Weight:** Monthly **Chest X-Ray: if required** **Physician evaluation:** whenever required | IP can be extended for maximum three months (maximum duration of IP – 6 months). | If the sputum /culture is positive in follow-up at any time during treatment, DST should be done as per presumptive DR-TB case | After completion of treatment the patients should be followed up with clinical and/or sputum examination at |
| **Extra Pulmonary TB** | In patients with extra-pulmonary tuberculosis the treatment response is best assessed clinically. The help of radiological and other relevant investigations may also be taken as above. | - Extension of IP or and/or CP in DS EPTB may be required in consultation with the specialist concerned.  
- Extension of IP DR-TB EPTB may be required in consultation with the specialist concerned.  
- Refer to guidelines for EPTB duration of treatment. | the end of 6, 12, 18 and 24 months. |
| **Pediatric TB** | In children, who are unable to produce sputum, the response to treatment may be assessed clinically. The help of radiological and other relevant investigations may also be taken. | Same as above | |
*Extension of IP in DR-TB patients

**MDR TB patients**

IP should be given for at least six months. After 6 months of treatment, the patient will be reviewed and the treatment changed to CP if the 4th or 5th month culture result in solid or liquid culture is negative respectively. If the 4th or 5th month culture result remains positive, the treatment is extended by 1 month. Extension of IP beyond 1 month will be decided on the results of sputum culture of 5th or 6th and 6th or 7th months. If the result of the 4th month culture is still awaited after 6 months of treatment, the IP is extended until the result is available, with further treatment being decided according to the culture result. The IP can be extended up to a maximum of 3 months after which the patient will be initiated on the CP irrespective of the culture result. The recommended duration for CP is 18 months.

**Schedule for sputum culture examinations for MDR-TB**

<table>
<thead>
<tr>
<th>IP extension</th>
<th>Intensive phase</th>
<th>Extension of IP (1-3 months)</th>
<th>Continuation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>3 4 5 6</td>
<td>-</td>
<td>9 12 15 18 21 24</td>
</tr>
<tr>
<td>1 month</td>
<td>3 4 5 6</td>
<td>7</td>
<td>10 13 16 19 22 25</td>
</tr>
<tr>
<td>2 months</td>
<td>3 4 5 6</td>
<td>7 8</td>
<td>11 14 17 20 23 26</td>
</tr>
<tr>
<td>3 months</td>
<td>3 4 5 6</td>
<td>7 8 9</td>
<td>12 15 18 21 24 27</td>
</tr>
</tbody>
</table>

* For MDR TB with additional drug resistance (including XDR TB) patients and XDR-TB IP extension can be upto 1-6 months.

**MDR TB with additional drug resistance (including XDR TB) patients**

The change from IP to CP will be done only after achievement of culture conversion i.e., 2 consecutive negative cultures taken at least one month apart. In case of delay in culture conversion, the IP can be extended from 6 months up to a maximum of 12 months. In case of extension, the DR -TR Centre Committee, which will be responsible for initiating and monitoring the regimen for XDR TB, can decide on administering second line injectable intermittently (3 times/week) for the months 7 to 12. In case of extension of IP, the follow up culture months will shift by every month of extension of IP

**Mono/pol/yo DR TB patients**

IP should be given for at least 3 months. After 3 months of treatment, the patient will be reviewed. If after the 3rd month smear result remains positive, the sputum sample is sent for genotypic DST to Rifampicin by CBNAAT or LPA and Liquid/solid culture & DST to see for resistance amplification. Shifting of IP to CP will be based on result of culture. The IP can be extended up to a maximum of 3 months after which the patient will be initiated on the CP irrespective of the culture result. The recommended duration for CP is 9 months.

At any time during treatment, if and when the results of additional DST are available, the patient must be referred to the DR TB center for complete clinical review by the committee and possible treatment modification.
Contact investigation

- All close contacts, especially household contacts should be screened for TB.
- In case of paediatric TB patients, reverse contact tracing for search of any active TB case in the household of the child must be undertaken.
- Particular attention should be paid to contacts with the highest susceptibility to TB infection

All close contacts of DR-TB cases should be identified through contact tracing and evaluated for active TB disease as per RNTCP guidelines. If the contact is found to be suffering from pulmonary TB disease irrespective of the smear results, he/she will be identified as an “Presumptive MDR-TB”. The patient will be initiated on regimen for new or previously treated case based on their history of previous anti-TB treatment. Simultaneously two sputum samples will be transported for culture and DST to a RNTCP-certified C&DST laboratory.

Isoniazid Preventive Therapy

Children are more susceptible to TB infection, more likely to develop active TB disease soon after infection, and more likely to develop severe forms of disseminated TB. Children < 6 years of age, who are close contacts of a TB patient, should be evaluated for active TB by a medical officer/paediatrician. After excluding active TB he/she should be given INH preventive therapy irrespective of their BCG or nutritional status. The dose of INH for preventive therapy is 10 mg/kg body weight administered daily for a minimum period of six months. The INH tablets should be collected on monthly basis. The contacts should be closely monitored for TB symptoms. In addition to above, INH preventive therapy should be considered in following situation:-

- For all HIV infected children who either had a known exposure to an infectious TB case or are Tuberculin skin test (TST) positive (>=5mm induration) but have no active TB disease.
- All TST positive children who are receiving immunosuppressive therapy (e.g. Children with nephrotic syndrome, acute leukemia, etc.).
- A child born to mother who was diagnosed to have TB in pregnancy should receive prophylaxis for 6 months, provided congenital TB has been ruled out. BCG vaccination can be given at birth even if INH preventive therapy is planned.

Close contacts of index cases with proven DR-TB should be monitored closely for signs and symptoms of active TB as isoniazid may not be prophylactic in these cases. Although alternative prophylaxis treatments have been suggested, there is no consensus regarding the choice of the drug(s) and the duration of treatment. Prompt treatment of MDR-TB is the most effective way of preventing the spread of infection to others. The following measures should be taken to prevent spread of DR-TB infection:
1. Early diagnosis and appropriate treatment of MDR-TB cases;
2. Screening of contacts as per RNTCP guidelines

Further research into effective and non-toxic chemoprophylaxis in areas of high MDR-TB prevalence is required.

Death Audit

The Medical Officer should conduct an in-depth audit of all the deaths occurring amongst the TB patients irrespective of initiation of treatment. Similarly, DTO should conduct death review of all MDR-TB patients died. This would be beneficial understanding the causes leading to the deaths and guide the programme in taking appropriate action to prevent them.
Prevention and management of adverse drug reactions

Most TB patients on first line drugs complete their treatment without any significant adverse drug effects. However, a few patients do experience adverse effects and some of the drug induced side effects can be prevented. Moreover, many second line drugs are associated with more side effects during long duration of treatment. It is therefore important that patients be clinically monitored during treatment so that adverse effects can be detected promptly and managed properly. All Health personnel should monitor patients about adverse drug effects and inform patients to report to health system in case of any of the side effects. Health-care workers need to be informed and trained about the methodology and channels for reporting ADRs.

Adverse effects of Anti TB drugs

Anti-TB treatment with first-line drugs is generally safe and well tolerated. Side effects to anti-TB drugs are common. Trivial side effects may lead to reduced compliance with treatment. These adverse effects must be recognized early, to reduce associated morbidity and mortality. Following table shows the side effects of essential first line anti TB drugs :-

<table>
<thead>
<tr>
<th>Drug</th>
<th>Main effects</th>
<th>Rare effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>Peripheral neuropathy</td>
<td>Convulsions</td>
</tr>
<tr>
<td></td>
<td>Skin rash</td>
<td>Psychosis</td>
</tr>
<tr>
<td></td>
<td>Hepatitis</td>
<td>Arthralgia</td>
</tr>
<tr>
<td></td>
<td>Sleepiness and lethargy</td>
<td>Anaemia</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal: abdominal pain, nausea, vomiting</td>
<td>Osteomalacia</td>
</tr>
<tr>
<td></td>
<td>Hepatitis</td>
<td>Pseudomembranous colitis</td>
</tr>
<tr>
<td></td>
<td>Generalised cutaneous reactions</td>
<td>Pseudoadrenal crisis</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenic purpura</td>
<td>Acute renal failure</td>
</tr>
<tr>
<td></td>
<td>Arthralgia</td>
<td>Haemolytic anaemia</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Hepatitis</td>
<td>Cutaneous reactions</td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal</td>
<td>Sideroblastic anaemia</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Retrobulbar neuritis</td>
<td>Generalised cutaneous reactions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Arthralgia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peripheral neuropathy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hepatitis (very rare)</td>
</tr>
</tbody>
</table>
Following table shows the side effects of second line anti TB drugs:

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Injectables</strong></td>
<td></td>
</tr>
<tr>
<td>Kanamycin</td>
<td>• Ototoxicity</td>
</tr>
<tr>
<td>/ Capreomycin</td>
<td>• Nephrotoxicity</td>
</tr>
<tr>
<td></td>
<td>• Vertigo</td>
</tr>
<tr>
<td></td>
<td>• Electrolyte imbalance</td>
</tr>
<tr>
<td><strong>Quinolones</strong></td>
<td></td>
</tr>
<tr>
<td>Ofloxacin,</td>
<td>• Gastro Intestinal symptoms: diarrhoea, vomiting, and abdominal pain</td>
</tr>
<tr>
<td>Levofloxacin,</td>
<td>• Central nervous system (CNS): dizziness and convulsions</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>• Phototoxicity and photosensitivity</td>
</tr>
<tr>
<td></td>
<td>• Tendinopathy and tendinitis</td>
</tr>
<tr>
<td></td>
<td>• Skin rash</td>
</tr>
<tr>
<td></td>
<td>• Cardiotoxicity – QT prolongation</td>
</tr>
<tr>
<td></td>
<td>• Arthralgia</td>
</tr>
<tr>
<td><strong>Ethionamide</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gastro-intestinal: epigastric discomfort, anorexia, nausea, metallic taste,</td>
</tr>
<tr>
<td></td>
<td>• excessive salivation, and sulfurous belching</td>
</tr>
<tr>
<td></td>
<td>• Psychiatric: hallucination and depression</td>
</tr>
<tr>
<td></td>
<td>• Hepatitis</td>
</tr>
<tr>
<td></td>
<td>• Hypothyroidism and goitre with prolonged administration</td>
</tr>
<tr>
<td></td>
<td>• Gynaecomastia, menstrual disturbances, impotence, acne, headache, and peripheral</td>
</tr>
<tr>
<td></td>
<td>• neuropathy</td>
</tr>
<tr>
<td><strong>Cycloserine</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• CNS: dizziness, slurred speech, convulsions, headache, tremor, and insomnia</td>
</tr>
<tr>
<td></td>
<td>• Psychiatric: confusion, depression, altered behaviour, and suicidal tendency</td>
</tr>
<tr>
<td></td>
<td>• Hypersensitivity reaction</td>
</tr>
<tr>
<td><strong>PAS</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gastro-intestinal: anorexia, nausea, vomiting, and abdominal discomfort</td>
</tr>
<tr>
<td></td>
<td>• Skin rash</td>
</tr>
<tr>
<td></td>
<td>• Hepatic dysfunction</td>
</tr>
<tr>
<td></td>
<td>• Hypokalemia</td>
</tr>
<tr>
<td></td>
<td>• Hypothyroidism and goitre with prolonged administration</td>
</tr>
</tbody>
</table>

**Management of ADRs**

**What to do if symptoms of adverse effects occur**

If symptoms of adverse effects occur the following should be done:

- the dose of drugs should be checked
- all other causes of symptoms should be excluded
- the seriousness of the adverse effects should be estimated
- the adverse effects should be registered
- the drugs may need to be stopped and should eventually be reintroduced gradually when symptoms disappear
- development of drug resistance should be avoided.

A symptom-based approach to the management of the most common adverse effects is adopted. These side effects are classified as major or minor. In general, a patient who develops minor adverse effects should continue the TB treatment and be given symptomatic treatment. If a patient develops a major side-effect, the responsible drug or the entire regimen may need to be stopped and the patient should be urgently referred to a clinician or health care facility for further assessment and treatment. Patients with major adverse reactions should be managed in a hospital. States need to identify such facilities with sufficient infection control measures and expertise. In DR-TB patients, the DR-TB committee needs to be involved in the management and modification of the regimen if required.

Management of ADRs by medical practitioners and health workers are detailed in Annexure 9 & 10

**Pharmacovigilance in TB control programme**

Pharmacovigilance is defined by the World Health Organization (WHO) as the “science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem”.

It is a fundamental activity to inform the management of patient safety measures in health care. Pharmacovigilance is a *public health surveillance activity*. There are 3 methods for reporting on pharmacovigilance activities:

- Spontaneous reporting- Spontaneous (or voluntary) reporting means that no active measures are taken to look for adverse effects other than the encouragement of health professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. This is the most common form of pharmacovigilance, sometimes termed passive reporting

- Targeted reporting- It focuses on capturing ADRs in a well-defined group of patients on treatment. Health professionals in charge of the patients are sensitized to report specific safety concerns.

- Active surveillance- It is a pro-active efforts made to elicit adverse events. Events detected by asking patients directly, screening patient records, laboratory & clinical tests. It is best done prospectively

Causality assessment- “Estimating the probability of a relationship between exposure to a medicine and the occurrence of an adverse reaction”. For assessing the causality the causality assessment committee. Establishing causality is a process which begins by examining the relationship between the medicine and the event. Two basic questions need to be addressed separately:

- Is there a convincing relationship between the drug and the event?
- Did the drug actually cause the event?

The relationship of a single case-report can be established, but it may not be possible to establish a firm opinion on causality until a collection of such reports is assessed or new knowledge is gained. Causality for individual reports, even those with a close relationship, can seldom be established beyond doubt and our assessments are based on probability. A causality assessment should be seen as provisional and subject to change in the light of further information on the case, or new knowledge coming from other sources. For details “a practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis” by WHO may be referred.
Under the Pharmacovigilance Programme of India (PvPI) set up by the Ministry of Health and Family Welfare (MoHFW), Govt. of India in July 2010 routine reporting and monitoring of ADRs will be continued. Simultaneously, the pharmacovigilance activity will be implemented in phase-wise manner.

Priority is given to establishing pharmacovigilance at DR-TB centres for drug resistant Cases. The DR-TB centres would be linked with ADR monitoring centres established under PvPI in medical colleges to initiate reporting of ADR in systematic manner. With introduction of daily anti-TB treatment regimen priority will be given to establish pharmacovigilance at ART centres for TB-HIV patients. It will be further expanded in districts / health institutions along with expansion of daily regimen to other TB patients. The standardized suspected ADR reporting form (Annexure 11) and needs to be filled by the treating doctor.

**Treatment in special situations**

**TB in Pregnant and Lactating women**

Before initiating treatment for tuberculosis, women of childbearing age should be asked about current or planned pregnancy and counseled appropriately. A successful treatment of TB is important for successful outcome of pregnancy. With the exception of streptomycin, the first line anti-TB drugs are safe for use in pregnancy. Streptomycin is ototoxic to the fetus and should not be used during pregnancy.

A breastfeeding woman should receive a full course of TB treatment. Correct chemotherapy is the best way to prevent transmission of TB to baby. Breast feeding has to be continued. After ruling out active TB, the baby should be given 6 months of isoniazid preventive therapy, followed by BCG vaccination. Breast feeding should not be discouraged. The mother should be advised about cough hygiene measures such as covering the nose and mouth while coughing, sneezing or any act which can produce sputum droplets. Mothers receiving INH and their breastfed infants should be supplemented with vitamin B6 (pyridoxine), recommended dose of Pyridoxine in infants is 5 mg/day.

**DR-TB in pregnancy**

Teratogenicity has been demonstrated with only some of the drugs used to treat MDR-TB. Women of child bearing age identified as presumptive MDR TB case should be advised to use a reliable and appropriate contraceptive method till the results of culture and DST are available. And if a woman is diagnosed with DR-TB and receiving second line treatment, she should be intensively counselled to use birth control measures because of the potential risk to both mother and foetus. All women of childbearing age should be tested for pregnancy as part of the pre-treatment evaluation and whilst on treatment if there is a history of amenorrhea of any duration. MDR-TB patients found to be pregnant prior to treatment initiation or whilst on treatment are evaluated in consultation with a Gynaecologist/Obstetrician taking into consideration the following factors:

- Risks and benefits of MDR-TB treatment
- Severity of the MDR-TB
- Gestational age
- Potential risk to the foetus

Further management of MDR-TB patients who are pregnant prior to initiation of treatment or whilst on treatment are based on the duration of pregnancy:

- If the duration of pregnancy is <20 weeks, the patient should be advised to opt for a Medical Termination of Pregnancy (MTP) in view of the potential severe risk to both the mother and foetus. If the patient is willing, she should be referred to a Gynaecologist/Obstetrician for MTP following which treatment can be initiated (if the patient has not started treatment) or continued (if the patient is already on treatment) by the DR-TB Centre Committee.
• For patients who are unwilling for MTP or have pregnancy of >20 weeks (making them ineligible for MTP), the risk to the mother and foetus needs to be explained clearly and a modified Regimen for MDR TB should be started as detailed below:
  
  - For patients in the first trimester (< 12 weeks), Kanamycin and Ethionamide are omitted from the regimen and PAS is added.
  - For patients who have completed the first trimester (>12 weeks), Kanamycin is replaced with PAS. Post-partum, PAS may be replaced with Kanamycin and continued until the end of the Intensive Phase.

Pregnant MDR-TB patients need to be monitored carefully both in relation to the treatment and the progress of the pregnancy. This approach should lead to good results, since the patient should be smear-negative at the time of parturition, and mother and infant do not need to be separated. Breast-feeding should be encouraged as long as the patient is sputum negative.

The management of MDR-TB patients with pregnancy is summarised in the flow chart:

**TB and Contraceptive pills usage**

As Rifampicin is a potent inducer of hepatic enzymes, the protective efficacy of oral contraceptive pills may be decreased. Oral contraceptives might have decreased efficacy due to vomiting and drug interactions with second line anti-TB drugs. Hence, women suffering from TB and using contraceptive pills should be advised to use some alternative anti-contraception method. Use of barrier methods (Condoms/diaphragms), IUDs (CuT) or depot-medroxyprogesterone (Depo-provera) are recommended based on individual preference and eligibility.
Management of TB in patients with liver disorders

Patients with hepatitis virus carriage, a past history of acute hepatitis, current excessive alcohol consumption can receive the usual TB regimens provided that there is no clinical evidence of chronic liver disease. However, hepatotoxic reactions to anti-TB drugs may be more common among these patients and should therefore be anticipated. In patients with unstable or advanced liver disease, liver function tests should be done at the start of treatment. If the liver disorder is severe, lesser hepatotoxic drugs have to be used. Expert consultation is advisable in treating patients with advanced or unstable liver disease. Clinical monitoring (and liver function tests, if possible) of all patients with pre-existing liver disease should be performed during treatment. If the serum alanine aminotransferase level is more than 3 times normal before the initiation of treatment, the following regimens should be considered:

- **Containing two hepatotoxic drugs:**
  9 months of isoniazid and rifampicin, plus ethambutol (until or unless isoniazid susceptibility is documented);  
  2 months of isoniazid, rifampicin, streptomycin and ethambutol, followed by 7 months of isoniazid and rifampicin;  
  6–9 months of rifampicin, pyrazinamide and ethambutol.

- **Containing one hepatotoxic drug:**
  2 months of isoniazid, ethambutol and streptomycin, followed by 10 months of isoniazid and ethambutol

- **Containing no hepatotoxic drugs:**
  18–24 months of streptomycin, ethambutol and a fluoroquinolone.

**DR-TB in patients with pre-existing liver disease**

Pyrazinamide, PAS and Ethionamide are potentially hepatotoxic drugs. Hepatitis occurs rarely with the fluoroquinolones. The potential for hepatotoxicity is increased in elderly, alcoholics and in patients with pre-existing liver disease. In general, most of second line drugs can be safely used in presence of mild hepatic impairment, as they are relatively less hepatotoxic than the first-line drugs. However, pyrazinamide and ethionamide should be avoided in such patients. Once a patient on second line drugs develops hepatitis, other aetiologies should also be excluded such as viral hepatitis, alcoholic hepatitis, drug induced hepatitis by non-TB drugs etc. The further management should be on the same guidelines as in non-MDR-TB patients. MDR patients having deranged liver function test (LFT) during pre-treatment evaluation should be strictly monitored through monthly LFTs while on treatment. However routine LFT is not recommended in all cases.

**TB patient with renal failure and severe renal insufficiency**

Patients suffering from Chronic Kidney Diseases (CKD) are at an increased risk of developing Tuberculosis. Active TB should be excluded in patients with CKD by appropriate investigations in patients who have an abnormal chest x-ray or a history of prior pulmonary or extrapulmonary TB that has been either inadequately or not previously treated. Chemoprophylaxis in standard doses should be given. TB should be considered in all patients with unexplained systemic or system-specific symptoms as extrapulmonary TB is common, particularly in patients on dialysis, with peritoneal TB being common in patients on chronic ambulatory peritoneal dialysis.

Any patient with active TB, either pulmonary or extrapulmonary, should receive standard chemotherapy agents, albeit with dose interval modifications where appropriate. Isoniazid and rifampicin are eliminated by biliary excretion, so no change in dosing is necessary. There is significant renal excretion of ethambutol and metabolites of pyrazinamide, and doses should therefore be adjusted. For patients with stages 4 and 5 chronic renal disease and on hemodialysis, dosing intervals should be increased to three times weekly for ethambutol, pyrazinamide and the aminoglycosides.
Treatment can be given immediately after haemodialysis to avoid premature drug removal. With this strategy there is a possible risk of raised drug levels of ethambutol and pyrazinamide between dialysis sessions. Alternatively, treatment can be given 4 to 6 hours before dialysis, increasing the possibility of premature drug removal but reducing possible ethambutol or pyrazinamide toxicity. Three times per week administration of these two drugs at the following doses is recommended: pyrazinamide (25 mg/kg), and ethambutol (15 mg/kg). These doses are the ones used in daily regimens. While receiving isoniazid, patients with severe renal insufficiency or failure should also be given pyridoxine in order to prevent peripheral neuropathy. Because of an increased risk of nephrotoxicity and ototoxicity, streptomycin should be avoided in patients with renal failure. If streptomycin must be used, the dosage is 15 mg/kg, two or three times per week, to a maximum of 1 gram per dose, and serum levels of the drug should be monitored. In post renal transplant cases, Rifampicin in particular can interact with immunosuppressive regimens, increasing the chance of graft rejection, and doses of mycophenolate mofetil, tacrolimus and cyclosporine may need adjustment. Corticosteroid doses should be doubled in patients receiving rifampicin.

**DR-TB in patients with renal impairment**

Renal insufficiency due to longstanding TB disease itself, previous use of aminoglycosides or concurrent renal disease is not uncommon. Great care should be taken in the administration of second-line drugs in patients with renal impairment. Consideration needs to be taken that MDR-TB patients require aminoglycosides for 6 months or more. In patients with mild renal impairment, the dose of aminoglycosides may be reduced. In the presence of severe renal failure, the aminoglycoside therapy should be discontinued and replaced with other potent non-nephrotoxic antituberculosos drugs. Other drugs, which also might require dose or interval adjustment in presence of mild to moderate renal impairment, are: Ethambutol, Quinolones, Cycloserine and PAS. In the presence of severe renal impairment many other drugs may also require adjustments (refer table as below).
## Adjustment of anti-TB drugs in renal insufficiency*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended dose and frequency for patients with creatinine clearance &lt; 30 ml/min or for patients receiving haemodialysis (unless otherwise indicated dose after dialysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>25-35 mg/kg per dose three times per week (not daily)</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>15-25 mg/kg per dose three times per week (not daily)</td>
</tr>
<tr>
<td>Rifabutin</td>
<td>Normal dose can be used, if possible monitor drug concentrations to avoid toxicity.</td>
</tr>
<tr>
<td>Rifapentpine</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Streptomycin</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
<tr>
<td>Capreomycin</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>12-15 mg/kg per dose two or three times per week (not daily)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>600-800 mg per dose three times per week (not daily)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>750-1000 mg per dose three times per week (not daily)</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Cycloserine</td>
<td>250 mg once daily, or 500 mg / dose three times per week</td>
</tr>
<tr>
<td>Terizidone</td>
<td>Recommendations not available</td>
</tr>
<tr>
<td>Prothionamide</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Ethionamide</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Para-aminosalicylicacid</td>
<td>4 g/dose, twice daily maximum dose</td>
</tr>
<tr>
<td>Bedaquiline</td>
<td>No dosage adjustments required in patients with mild to moderate renal impairment (dosing not established in severe renal impairment, use with caution).</td>
</tr>
<tr>
<td>Linezolid</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Clofazimine</td>
<td>No adjustment necessary</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate</td>
<td>For creatinine clearance 10-30 ml/min dose 1000 mg as amoxicillin component twice daily; For creatinine clearance &lt;10 ml/min dose 1000 mg as amoxicillin component once daily</td>
</tr>
<tr>
<td>Imipenem / cilastin</td>
<td>For creatinine clearance 20-40 ml/min dose 500 mg every 8 hours; For creatinine clearance &lt;20 ml/min dose 500 mg every 12 hours</td>
</tr>
<tr>
<td>Meropenem</td>
<td>For creatinine clearance 20-40 ml/min dose 750 mg every 12 hours; For creatinine clearance &lt;20 ml/min dose 500 mg every 12 hours</td>
</tr>
<tr>
<td>High dose isoniazid</td>
<td>Recommendations not available</td>
</tr>
</tbody>
</table>


**Estimated creatinine clearance calculations:**

*Men*:  Ideal Body Weight (kg) x (140-age) / 72 x serum creatinine (mg/dl)

*Women*: 0.85 x Ideal Body Weight (kg) x (140-age) / 72 x serum creatinine (mg/dl)
**TB in patients with seizure disorders**
The use of isoniazid and rifampicin may interfere with many of the anti-seizure medications. Drug interactions should be checked before their use. High dose isoniazid also carries a high risk of seizure and should be avoided in patients with active seizure disorders.

The prophylactic use of oral pyridoxine (vitamin B6) can be used in patients with seizure disorders to protect against the neurological adverse effects of isoniazid or cycloserine. The suggested prophylactic dose for at risk patients on isoniazid is 10 to 25 mg/day and for patients on cycloserine is 25 mg of pyridoxine for every 250 mg of cycloserine daily. The optimal prophylactic dose of pyridoxine for children has not been established, nonetheless 1–2 mg/kg/day has been recommended in some reports with a usual range of 10–50 mg/day for paediatric patients at risk for neurological sequel.

**DR-TB in patients with seizure disorders**
Some patients requiring treatment for DR-TB will have a past or present medical history of a seizure disorder. The first step in evaluating such patients is to determine whether the seizure disorder is under control and whether the patient is taking anti-seizure medication to control the disorder. If the seizures are not under control, initiation or adjustment of anti-seizure medications will be needed prior to the start of DR-TB therapy. In addition, if other underlying conditions or causes for seizures exist, they should be corrected.

Among second line drugs, Cycloserine, Ethionamide and fluoroquinolones have been associated with seizures, and hence should be used carefully amongst MDR-TB patients with history of seizures. Pyridoxine should be given with Cycloserine to prevent seizures. Cycloserine should however be avoided in patients with active seizure disorders that are not well controlled with medication. In cases where no other drug is appropriate, Cycloserine can be given and the anti-seizure medication adjusted as needed to control the seizure disorder. The risk and benefits of using Cycloserine should be discussed with the patient and the decision on whether to use Cycloserine are made together with the patient.

Antiepileptic drugs may have drug interactions with Cycloserine and fluoroquinolones. Hence close monitoring of serum levels of anti-epileptic drugs should be done. One should remember that TB itself might involve central nervous system and may cause seizures. However when seizures are present for the first time during anti-TB therapy, they are likely to be the result of an adverse effect of one of the anti-TB drugs.

**DR-TB in patients with psychosis**
For DR-TB patients with a concurrent psychiatric illness, it is advisable to have an evaluation carried out by a psychiatrist before the start of treatment for DR-TB. The initial evaluation documents any pre-existing psychiatric condition and establishes a baseline for comparison if new psychiatric symptoms develop while the patient is on treatment. Any identified psychiatric illness at the start or during treatment should be fully addressed. There is a high baseline incidence of depression and anxiety in patients with DR-TB, often connected with the chronicity and socioeconomic stress factors related to the disease. If a health care worker with psychiatric training is not available, the treating healthcare provider should document any psychiatric conditions the patient may have at the initial evaluation.

Treatment with psychiatric medication, individual counselling, and/or group therapy may be necessary to manage the patient suffering from a psychiatric condition or adverse psychiatric effect due to medication. Group therapy has been very successful in providing a supportive environment for DR-TB patients and may be helpful for patients with or without psychiatric conditions (adequate measures to prevent infection risk should be in place for the group therapy). Fluoroquinolones and Ethionomide have been associated with psychosis. Pyridoxine prophylaxis may minimize risk of neurologic and psychiatric adverse reactions.
Cycloserine may cause severe psychosis and depression leading to suicidal tendencies. However the use of Cycloserine is not absolutely contraindicated for the psychiatric patient. Adverse effects of Cycloserine may be more prevalent in the psychiatric patient, but the benefits of using this drug often outweigh the potential higher risk of adverse effects. Close monitoring is recommended if Cycloserine is used in patients with psychiatric disorders.

If patient on Cycloserine therapy develops psychosis, anti-psychotic treatment should be started and Cycloserine therapy should be temporarily suspended. Once symptoms resolve and patient is stabilized Cycloserine therapy may be resumed. Such patients may require anti-psychotic treatment till anti-TB treatment is completed. When any patient on MDR-TB treatment develops psychosis, other aetiologies such as psycho- social stresses, depression, hypothyroidism, illicit drug and alcohol use, should also be looked for.

All healthcare workers treating drug-resistant TB should closely work with a psychiatrist and have an organized system for psychiatric emergencies. Psychiatric emergencies include psychosis, suicidal ideation, and any situation involving the patient's being a danger to him/her self or others. Mechanisms to deal with psychiatric emergencies (often inpatient psychiatric hospital admissions) should be available on twenty-four hours basis. Proper infection control measures must be taken for the smear-positive patient who requires any hospitalization.

Extra pulmonary TB
The burden of EPTB ranges from 15-20% of all TB cases in HIV-negative patients while among PLHIV, it accounts for 40-50% of new TB cases. With advent of diagnostics cases of drug-resistant EPTB are likely to be identified more in the country.

All EPTB patients should be tested for HIV. All patients suspected of EPTB should have clinical assessment for active PTB. All patients should receive an appropriate treatment regimen, and the provider should monitor adherence and address factors leading to interruption/discontinuation of treatment. All patients with a diagnosis of EPTB should be risk-assessed for drug resistance prior to starting treatment, and drug susceptibility testing should be available for all patients at risk of drug-resistant tuberculosis.

Extra pulmonary TB should be treated with the same regimens as pulmonary TB. The duration of continuation phase may be extended by 3 to 6 months in special situations like TB meningitis, Bone & Joint TB, Spinal TB with neurological involvement and neuro- tuberculosis. Unless drug resistance is suspected, adjuvant corticosteroid treatment is recommended for TB meningitis and pericarditis. In tuberculous meningitis, ethambutol should be replaced with streptomycin.

Although sometimes required for diagnosis, surgery plays little role in the treatment of extra pulmonary TB. It is reserved for management of late complications of disease such as hydrocephalus, obstructive uropathy, constrictive pericarditis and neurological involvement from Pott's disease (spinal TB). For large, fluctuant lymph nodes that appear to be about to drain spontaneously, aspiration or incision and drainage appear beneficial. For further details on management of EPTB, refer to Index-TB guidelines on management of EPTB.

Treatment regimen and schedule for EP MDR-TB cases will remain the same as for pulmonary MDR-TB. EP MDR-TB patients will undergo all those pre-treatment investigations as done for pulmonary MDR-TB patients. In addition, ultrasound of abdomen of the patient will also be done, if necessary, to rule out involvement of other organs and abdominal nodes. Unlike microbiological follow up examination schedule in pulmonary DR-TB, culture from the affected EPTB site can be done only till the specimen is available. The follow up is mainly based on clinical parameters.
Clinical Monitoring and follow up of DR-TB patients:
1. Weight Gain  
2. Decrease or increase in symptoms (e.g. healing of ulcer / scrofuloderma)  
3. Increase or Regression in size of nodes (possibility of Immune Reconstitution Inflammatory Syndrome (IRIS) should be considered and differentiated from disease progression)  
4. Appearance of new nodes  
5. If chest symptomatic, monthly sputum for AFB and chest X-ray (to rule out pulmonary involvement)  
6. Other Extra-pulmonary sites should be monitored (USG abdomen if necessary)  
7. Serum Creatinine – monthly for the first three months of treatment and then quarterly till the patient receives Kanamycin and further when clinically indicated  
8. Liver function test – as clinically indicated  
9. USG -abdomen – if necessary  
10. Monitoring for drug adverse reactions

Treatment outcome will depend on availability of culture reports of specimens taken from affected site, treatment completion and clinical improvement of the patient.

Hospitalization
The usual mode of TB treatment is domiciliary, but in patients with pneumothorax or large accumulations of pleural fluid leading to breathlessness; massive haemoptysis etc. the patients might need hospitalization. These patients can be managed in general hospitals preferably in wards where adequate air borne infection control measures are taken to prevent the spread.

Role of surgery in management of MDR-TB
In DR-TB patients with localized disease, surgery, as an adjunct to chemotherapy, can improve outcomes provided skilled thoracic surgeons and excellent post-operative care are available. When unilateral resectable disease is present, surgery should be considered for the following cases:
• Absence of clinical or microbiological response to chemotherapy despite six to nine months of treatment with effective anti-tuberculosis drugs;  
• High risk of failure or relapse due to high degree of resistance or extensive parenchymal involvement;  
• Morbid complications of parenchymal disease e.g. haemoptysis, bronchiectasis, bronchopleural fistula, or empyema;  
• Recurrence of positive culture status during course of treatment; and  
• Relapse after completion of anti-tuberculosis treatment.

If surgical option is under consideration at least six to nine months of chemotherapy is recommended prior to surgery.
Latent Tuberculosis Infection (LTBI)
Latent tuberculosis infection (LTBI) is the presence of Mycobacterium tuberculosis in the body without signs and symptoms, or radiographic or bacteriologic evidence of tuberculosis (TB) disease. Studies have demonstrated that Isoniazid (INH) taken for at least 6 months in persons with LTBI reduced subsequent TB incidence by 25 to 92 per cent, the differences in effectiveness largely explained by differences in treatment completion. Recently WHO has published detailed guidelines for management of LTBI. (WHO Guidelines on the management of latent tuberculosis infection) There was consensus of the WHO Panel on the equivalence of 6-month INH, 9-month INH, and 3-months once a week Rifapentine plus high dose INH as treatment for LTBI.

India, with one-fourth of the global burden of TB, has 40 per cent of the population infected with M.Tb. Treating 40 per cent of the population for LTBI based on Tuberculin Skin Test (TST) positivity or Interferon Gamma Release Assay is neither rational nor practicable, thus emphasizing the need for a focussed approach. In clinical situations, the most obvious group for LTBI treatment would include high-risk patients such as those receiving long term corticosteroids, immunosuppressants, HIV-infected and juvenile contacts of sputum-positive index cases.

Treatment of Nontuberculous Mycobacterial (NTM) Lung Diseases
Under programme conditions sometimes the report of culture examination shows presence of Nontuberculous Mycobacteria (NTM). NTM represent a broad array of organisms that have been isolated from soil and water, and exposure to these reservoirs is thought to be the source of human infection. A review of several studies observed that in India 1-4% of laboratory isolates among presumptive TB cases or presumptive MDR-TB cases are NTMs. In TB-HIV co-infected cases the probability of NTM may be increased. The clinician (DTO/MOPHI/DR-TB Committee etc.) should not ignore such reports. A careful clinical correlation is required in such cases as some of these patients may be wrongly put on MDR/XDR-TB regimen as these patients may be found to be resistant to all commonly used first line and second line anti-TB drugs. One should not diagnose NTM based on single culture report. In presence of NTM the commonly used molecular tests, such as LPA or CBNAAT will be negative, which should prompt the clinician to think of NTM. Such cases should be referred to DR-TB committee for further management through general health services. The American Thoracic Society (ATS) Guidelines (An Official ATS/IDSA Statement: Diagnosis, Treatment, and Prevention of Nontuberculous Mycobacterial Diseases) may be referred for the management of patients suffering from NTM infection.
Treatment outcomes
The treatment outcome definitions make a clear distinction between three types of patient groups (“cohorts”):

1. Patients treated for drug-susceptible TB;
2. Patients treated for RR-/MDR-TB/XDR-TB
3. Patients treated for mono-/poly- DR-TB

The groups are mutually exclusive. Any patient found to have DR-TB and placed on second-line treatment is removed from the rifampicin-susceptible TB treatment cohort. DR-TB patients who were not started on a Mono/Poly/MDR-TB regimen are assigned an outcome from those for rifampicin-susceptible TB. This means that the basic TB register and the Second-line TB treatment register need to be coordinated to ensure proper accounting of treatment outcomes.

Treatment outcomes for drug-susceptible TB patients

Cured: Microbiologically confirmed TB patients at the beginning of treatment who was smear or culture negative at the end of the complete treatment

Treatment completed: A TB patient who completed treatment without evidence of failure or clinical deterioration BUT with no record to show that the smear or culture results of biological specimen in the last month of treatment was negative, either because test was not done or because result is unavailable.

Treatment Success: TB patients either cured or treatment completed are accounted in treatment success

Failure: A TB patient whose biological specimen is positive by smear or culture at end of treatment.

Failure to Respond: A case of paediatric TB who fails to have microbiological conversion to negative status or fails to respond clinically / or deteriorates after 12 weeks of compliant intensive phase shall be deemed to have failed response provided alternative diagnoses/ reasons for non-response have been ruled out.

Lost to follow up: A TB patient whose treatment was interrupted for 1 consecutive month or more

Not Evaluated: A TB Patient for whom no treatment outcome is assigned. This includes former “transfer-out”

Treatment Regimen Changed: A TB patient who is on first line regimen and has been diagnosed as having DRTB and switched to drug resistant TB regimen prior to being declared as failed

Died: A patient who has died during the course of anti-TB treatment

Outcomes for RR-/MDR-TB and/or XDR-TB patients

Cure: Treatment completed as recommended by the national policy without evidence of failure AND three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase

Treatment completed: Treatment completed as recommended by the national policy without evidence of failure BUT no record that three or more consecutive cultures taken at least 30 days apart are negative after the intensive phase

Treatment success: The sum of cured and treatment completed.
Treatment failed: Treatment terminated or need for permanent regimen change of at least two or more anti-TB drugs in CP because of:
- Lack of microbiological conversion by the end of the intensive phase or
- Microbiological reversion in the continuation phase after conversion to negative or
- Evidence of additional acquired resistance to fluoroquinolones or second line injectable drugs or
- Adverse drug reactions (ADR)

Conversion and reversion
Conversion (to negative): culture is considered to have converted to negative when two consecutive cultures, taken at least 30 days apart, are found to be negative. In such a case, the specimen collection date of the first negative culture is used as the date of conversion.
Reversion (to positive): culture is considered to have reverted to positive when, after an initial conversion, two consecutive cultures, taken at least 30 days apart, are found to be positive. For the purpose of defining Treatment failed, reversion is considered only when it occurs in the continuation phase.
Died: A patient who dies for any reason during the course of treatment
Loss to follow up: A patient whose treatment was interrupted for one consecutive month or more
Not Evaluated - A patient for whom no treatment outcome is assigned.
Treatment Regimen Changed - An TB patient need for permanent regimen change of at least one or more anti-TB drugs prior to being declared as failed.

Outcomes for mono-/ poly-drug resistant TB patients
Cure: A microbiologically confirmed TB at the beginning of treatment who was culture-negative in the last month of treatment and on at least one previous occasion
Treatment completed: A patient who has completed treatment according to guidelines but does not meet the definition for cure or treatment failure due to lack of microbiological results.
Failure: Treatment terminated or need for permanent regimen change of at least two or more anti-TB drugs in CP because of:
- Evidence of additional acquired resistance to rifampicin, fluoroquinolone or second line injectable during treatment
- Severe ADR
- Culture positive during CP or at end of treatment
Died: A patient who dies for any reason during the course of M/XDR-TB treatment
Loss to follow up: A patient whose treatment was interrupted for one month or more for any reasons.
Not Evaluated - A DR-TB Patient for whom no treatment outcome is assigned, this includes former “transfer-out”.

Treatment outcome is defined by reviewing her/his Tuberculosis Treatment Card. The treatment outcome and the date the patient stopped treatment is written in the appropriate column in the Tuberculosis treatment card. The date on which the patient stopped treatment is the date of the last dose of drugs taken. Details of Treatment outcome should be updated in NIKSHAY.

The MO of the PHI should record the treatment outcome in the treatment card and sign it. The treatment card of the patients whose outcome has been declared should be handed over to the STS during his routine monthly visits. Every patient started on treatment has to be given one and only one treatment outcome.
TB Comorbidities

Several medical conditions are risk factors for TB and poor TB treatment outcomes. Similarly, TB can complicate course of some diseases. It is therefore important to identify these comorbidities in people diagnosed with TB in order to ensure early diagnosis and improved outcome. When these conditions are highly prevalent in the general population they can be important contributors to the TB burden. Consequently, reducing the prevalence of these conditions can help prevent TB. TB share underlying social determinants with many of these conditions. Addressing the social determinants of health is a shared responsibility across disease programmes and other stakeholders within and beyond the health sector.

TB and HIV

The primary impact of HIV on TB is that the risk of developing TB becomes higher in patients with HIV. Overall, HIV-infected persons have approximately an 8-times greater risk of TB than persons without HIV infection. The risk of TB in HIV-infected persons continues to increase as HIV disease progresses and CD4 cell count decreases. While anti-retroviral treatment can substantially decrease the risk of TB, this risk always remains higher than that in HIV negative individuals. Furthermore, among cured TB survivors with HIV infection, the risk of recurrent TB is also quite high.

Similarly, Tuberculosis is the most common opportunistic infection amongst HIV-infected individuals. It is a major cause of mortality among patients with HIV and poses a risk throughout the course of HIV disease.

The presentation of TB in the HIV-infected patient may vary with degree of immune suppression. The diagnosis of TB in PLHIV can be more difficult and may be confused with other pulmonary or systemic infections. As the HIV disease progresses and the individual become more immune-compromised, the clinical presentation is proportionately more likely to be extra-pulmonary or smear-negative than in HIV-uninfected TB patients. This can result in misdiagnosis or delays in diagnosis, and in turn, higher morbidity and mortality.

It is estimated that there are 2.1 million people living with HIV in India with an estimated adult HIV prevalence of 0.27% (range: 0.2%–0.4%). TB accounts for 25% of deaths among People Living with HIV and AIDS (PLHIV) in India. Although only 5% of incident TB patients are HIV-infected, in absolute terms it means more than 100,000 cases annually, ranks second in the world and accounts for about 10% of the global burden of HIV-associated TB. HIV positivity among PLHIV varies from states/districts in the country, the proportion of HIV positive among TB patients over 10% in high HIV burden states to up to 40% in some high burden districts.
NACP and RNTCP Coordination in India:
To mitigate the effect of dual burden of HIV and TB co-infection, the ministry of Health and Family Welfare, Government of India through its NACO and Central TB Division (Department of Health and Family Welfare) has been undertaking joint collaborative efforts since 2001. While joint HIV/TB activities started with differential strategies based on underlying HIV burden initially, the programme evolved over the years and currently implements uniform HIV/TB collaborative activities across the country. NACP and RNTCP have developed a policy of HIV/TB collaborative interventions based on experience gained during programme implementation in initial years. The mechanism for collaboration includes coordinated service delivery at field level, and oversight and advisory groups at the district level in the form District Coordination Committee chaired by District Collector. At the state level, a similar mechanism exists in the form of the State Technical Working Group chaired by Director Health Services and State Coordination Committee chaired by Principle Secretary Health. At the National level, TB-HIV coordination committee chaired by Additional Secretary, National AIDS Control Organization [NACO] and technical working group [NTWG] chaired by DDG regularly monitor and provide suggestions on key policy matters related to TB/HIV Collaborative activities. To enable effective coordination, joint trainings, standard recording and reporting, joint monitoring and evaluation and operational research are strategically implemented.

**Milestones of TB-HIV collaborative activities in India**
- 2001 - Basic HIV/TB activities started in six high-HIV burden states.
- 2003 - Pilot for HIV-TB cross-referral in four districts of Maharashtra.
  - Cross-referral started in six HIV high prevalence states.
- 2004 - Cross referral of activities expanded to eight additional states.
- 2005 - Joint training modules developed, joint surveillance initiated.
- 2007 - Pilot for Routine referral of TB patients for HIV testing and CPT.
  - National (policy) framework for TB/HIV developed.
- 2008 - National Framework revised.
  - All-India implementation of HIV-TB activities.
  - Intensified Package (IP) rolled out in nine states.
  - Intensified Package rolled out in eight more states.
  - Uniform activities at ART centers and ICTCs nationwide for intensified TB case finding and reporting, established.
- 2010 - Intensified package launched in 11 states.
- 2012 - Nationwide coverage achieved.
- 2013 - National Framework for HIV/TB collaborative activities in India developed

National Framework for HIV/TB in India:
Latest revision of National Framework Nov 2013 aimed to incorporate recent policy updates in NACP and RNTCP and align with respective national strategic plan for next 5 year along with recommendations in WHO HIV/TB policy guidelines 2011
The salient features are as below.

1. Emphasis on Integrated TB and HIV services e.g. HIV screening at RNTCP DMC.

2. Focus on early detection and early care:

   a. Early detection of TB in PLHIV:
      i. Early suspicion of TB—symptoms of any duration among PLHIV
      ii. Use of an expanded clinical algorithm for TB screening that relies on presence of four clinical symptoms (current cough, weight loss, fever or night sweats) instead of only cough, to identify patients with presumptive TB
      iii. Strengthen ICF at ART, Link ART centre (LAC) and Targeted intervention projects (TI) for High Risk Group (HRG) specially Injection Drug Users (IDU)
      iv. Offering upfront CBNAAT among presumptive TB cases among PLHIV
      v. Early detection HIV/TB

   b. Enhance HIV testing facilities in settings with lack of co-located HIV and TB testing facilities, by establishing HIV screening services using whole blood finger prick test (WB)
      i. Strengthen HIV testing of TB patients in high HIV prevalent settings by promoting establishment of Facility Integrated Counselling and Testing Centre (F-ICTC) where DMC exists
      ii. PITCamong patients being evaluated by diagnostic smear microscopy presumptive TB cases in high HIV prevalent settings

   c. Early Care:
      i. Promotion of ‘single window delivery services’ where all HIV/TB patients get their TB medications from the ART centres along with ART drugs.
      ii. Strengthened linkage of HIV/TB patients to ART centres through travel support by RNTCP as per NSP (2012-2017) etc.
      iii. ART for HIV infected TB cases irrespective of CD4 count
      v. Monitoring of timeliness of ART initiation through expanded ART reporting formats

3. Early detection and care of HIV infected Drug Resistant TB patients (DR-TB/HIV):

   i. Strengthen HIV testing in presumptive DR-TB cases (Criteria C)
   ii. Ensure access to culture and drug susceptibility testing for HIV infected TB patients
   iii. Prompt linkage of HIV infected DR-TB cases to ART centres
   iv. Prompt initiation of ART in HIV infected DR-TB cases

4. Prevention of TB among HIV infected adults and children:

   i. Implementation of IPT for all PLHIV (On ART + Pre-ART)
   ii. Strengthen implementation of air borne infection control strategies.

5. Strengthen HIV/TB activities among children and pregnant women

6. Promotion of participation of private, NGO, CBO health facilities and affected communities working with NACP and RNTCP to strengthen HIV/TB collaborative activities.
HIV Screening for TB Patients / Presumptive TB cases

1. Presumptive / Diagnosed TB patients coming to the ICTCs will be offered counselling and testing as per the norms and standard operating procedures of the National AIDS Control Programme (NACP).
2. All referrals will be recorded in the ICTC counselling register as referrals from RNTCP.
3. For patients with HIV positive results, the counselor will link the patient to the nearest ART centre available in the district/state. This will be done by giving a referral form and explaining the patient on how to access the centre. The patient will be given the contact details of the district programme managers for any assistance needed.
4. The counsellor will document the HIV status, date of HIV testing and PID number in the RNTCP laboratory form as a feedback to LT of DMC. The counselor will also assist the DMC LT to update the laboratory register with information on HIV status.

Intensified TB case finding (ICF) at ICTCs, ART and Community Support Centres (CSCs)

Intensified TB case finding at HIV care settings is an important strategy for early diagnosis of TB among PLHIV.

ICF at ICTCs
All ICTC clients should be screened by ICTC counsellors for presence of TB symptoms at every encounter (pre, post, or follow-up counselling). Clients who have symptoms or signs, irrespective of their HIV status, should be referred to RNTCP diagnostic and treatment facility located in same institution. Therefore, NACP and RNTCP promote establishing co-located facilities, for better coordination between the two programmes. Hence, as network of HIV testing facilities is being expanded, consideration should be given to establish them at sites, which already have RNTCP, designated microscopy centres (DMC).

The referrals of presumptive TB cases from ICTCs to TB diagnosis facility should be recorded on a line list (Annexure 12A) to facilitate exchange of information with RNTCP and track the client through the process of TB diagnosis and initiation of TB treatment. To streamline this process further, RNTCP programme staff should stay in touch with ICTC counsellors to complete the exchange of information in time. In addition, ICTC counsellors and RNTCP programme staff participate in monthly HIV/TB coordination meeting at district level to validate line-lists and Monthly HIV/TB reports (Annexure 12B) and resolve operational issues if any.

ICF at ART Centres

HIV-infected persons attending ART centres for pre-ART registration have a high prevalence of TB disease (6 to 8%). The incidence of TB among ART clients is also very high, even when on ART. Although ART reduces risk of incident TB, it remains many times higher compared to general population. In addition, HIV-infected clients having undiagnosed or untreated TB may seek care at ART centres and thus exposing other HIV-infected persons to the risk of acquiring TB. Therefore active efforts for intensified TB case finding (ICF) at ART centres is critical for early suspicion and detection of TB, linkage to treatment and thus for prevention of transmission of infection to other clients. The national ART guidelines clearly state that all patients coming to ART centres should be actively screened for opportunistic infections, particularly tuberculosis. All people living with HIV should be regularly screened for four symptoms viz., current cough of any duration, fever of any duration, significant weight loss or drenching night sweats, during every visit to a health facility and every contact with a health-care provider. Those with history of coughing blood and sputum and with any pulmonary abnormality in chest X-ray should also be evaluated for TB. Similarly, children living with HIV who have one or more of the following symptoms – failure to thrive, fever or cough of any duration or history of contact with a TB patient should be evaluated for TB.
Screening for TB is important regardless of whether the PLHIV is receiving IPT or ART. The presumptive TB cases identified at ART centres or Link ART centres should be prioritized and “fast-tracked” for evaluation by SMO/MO to minimize opportunities for airborne transmission of infection to other PLHIV.

PLHIVs suspected to have TB by MO, should be subjected to testing of sputum / appropriate specimen from a relevant extra-pulmonary site by CBNAAT at the nearest facility. CBNAAT is the frontline test for diagnosis of TB among PLHIV. If CBNAAT is not available, arrangements have to be made for collection and transportation of sputum specimen to the nearest CBNAAT site. If CBNAAT linkage is not available, then the patient should be evaluated with microscopy and Chest-X ray on the same day.

Clinically diagnosed TB and extra pulmonary TB is more common among people living with HIV and therefore a high level of suspicion is required. In the event of suspicion of Extra Pulmonary TB, the diagnostic algorithm as for HIV negative presumptive EPTB patients may be followed. Similarly, refer to diagnostic algorithm for paediatric pulmonary TB.

Preferably, PLHIVs should be offered TB and HIV diagnostic facility at the same premises as a “one-stop service” in order to reduce diagnostic delay and to link those not having any of the four symptom complex to IPT services.

In addition, the referrals presumptive TB cases should be recorded on an ART centre TB-HIV line list (Annexure 13 A) to facilitate coordination with RNTCP programme staff and to track the patient closely through the process of TB diagnosis and TB treatment initiation. It is also crucial that ART Centre staff members attend monthly HIV/TB coordination meeting. The HIV/TB monthly reporting format to be generated at ART centres is incorporated into the ART centre monthly report (CMIS) (Annexure 13 B).

Information of all HIV infected TB patients in HIV care should be recorded in the ART centre HIV/TB register (Annexure 13 C). These include TB patients detected by ART centre staff as well as those TB patients found HIV infected while on TB treatment and referred to ART centre by the RNTCP. TB-HIV register is an important monitoring tool to track timeliness of initiation of CPT and ART the TB treatment outcome to modify ARV regimens as per guidelines. It is also important that ART centre staff carry this register when they attend monthly HIV/TB coordination meeting to update information on TB treatment outcome from RNTCP staff and share information pertaining to CPT and ART with them for recording into RNTCP TB registers.

PLHIV diagnosed to be suffering from TB are presumptive MDR cases and need to follow the algorithm for diagnosis of drug resistant TB (Refer Section 5).

**ICF at Link ART Centres (LAC)**

The ICF activity is also implemented at all Link ART plus and Link ART centres in the country. As in ART centres LAC-Plus and LAC should 1) implement ICF using symptom screening on every encounter 2) promptly refer presumptive TB case to RNTCP diagnostic facilities, and 3) refer the patient to ART centre promptly if TB is detected for initiation of ART or modify current ARV regimen. Similar to ART centre, the LAC staff nurse /counsellor should maintain line-list, exchange with local RNTCP staff to seek information on TB diagnosis and treatment and complete the line-list.

The LAC Plus use same line-list format as the ART centre (Annexure 13 A) while at LAC the ICTC line-list format is used (since ICTC counsellor runs the LAC) (Annexure 12A). The completed line-list from LAC-plus is merged with ART centre line-list whereas that from LAC is merged into ICTC line-list for the same period and monthly report is generated accordingly. These mechanisms are designed considering operational feasibility but key point is if TB is detected among patients at LAC plus of LAC, they must be promptly referred to ART centre for further management.
ICF among HIV high risk groups (HRG)
Operational research conducted in high HIV prevalent states have shown that HRG’s like female sex workers (FSW), men having sex with men (MSM), injection drug users (IDU) etc. are more likely to have tuberculosis compared to general population. In addition, it is known that HIV prevalence among the HRG is several times higher than general population. While NACCP provides HIV prevention interventions for the HRG through its targeted interventions, the ICF provides an opportunity to provide additional services to this population. This intervention is likely to help in detection HIV/TB cases early and link to care support and treatment. Among the HRG’s, IDU have highest HIV prevalence therefore the programmes aim to provide ICF services and prompt linkage to care support and treatment to IDU as a priority.

ICF at Care and support centres:
TB symptom screening based on 4 symptom complex should also be done by counsellors and outreach workers at Care and support centre in collaboration with SACS.

Treatment of HIV-infected TB
Early diagnosis and effective treatment of TB among HIV-infected patients are critical for controlling the disease and minimizing the adverse impact of TB on the course of HIV. Hence, initiation of treatment is very important soon after the diagnosis of TB. Among HIV-infected persons, treatment of TB is same as that in the HIV-negative TB patients.

Anti-TB Treatment of HIV infected TB patients:
- Based on the clinical history and investigation reports ART MO will categorize patients as Rifampicin sensitive/ rifampicin sensitivity status not known/ clinically diagnosed TB cases, prior history of taking Anti-TB drugs (Cat I /Cat II) accordingly and initiate daily anti TB treatment in Fixed Dosage Combination as per RNTCP guidelines at ART Centre itself.
- All HIV-infected TB patients if not tested already should be tested for drug susceptibility before initiation of treatment. Staff nurse will refer the patient to the nearest drug resistant TB centre in coordination with to RNTCP and record the same in the line list as DRTB /Rif resistant patient. PLHIV with drug resistant TB should be managed by DR-TB center in consultation with ART centre.
- The STS of TU where ART Centre / CBNAAT site is located (nodal TU) will link the patient to the concerned TU based on the residence of the patient for TB treatment provision and follow up as per RNTCP guidelines. STS (nodal TU) will also be responsible to get the registration details from the concerned TU. Overall
- Responsibility of this linkage and coordination lies with District HIV –TB and PMDT coordinator.
- TB patients living with HIV infection should receive the same duration of TB treatment with daily regimen as HIV-negative TB patients.
- If drug sensitive TB patient and on second line ART, Rifampicin should be replaced with Rifabutin 300 mg three times a week or 150 mg daily.
- TB Treatment card for these patients will be prepared by staff nurse in duplicate and will be duly signed by medical officer. One copy of the TB treatment card is to be handed over to the patient. Patient will be registered, allotted TB Number and Nikshay ID by STS of the concerned TU as per the RNTCP guidelines within one month and nodal TU will be informed
• Pharmacist will maintain the inventory of stocks of Anti-TB drugs at ART centre. District HIV-TB and PMDT coordinator should ensure availability of adequate stock of Anti-TB drug and logistics in coordination with ART centre, District TB Officer, District Drug store pharmacist.

• RNTCP will identify local treatment supporter for all HIV –TB co-infected patients. Anti TB treatment will be supervised by the local treatment supporter and any adverse drug reactions should be informed immediately to local medical officer at PHI and ART medical officer.

• Regular follow up of the patients, testing for sputum as per RNTCP Guidelines and adherence to ATT & ART treatment is to be ensured by the treatment supporter, STS, STLS, ART MO. ART Counsellor should ensure proper counselling in all the HIV-TB co-infected patients regarding adherence and possible side effects to ART and ATT.

• A mechanism of ensuring and checking adherence has been instituted by sending a missed call by patient to pre-printed phone numbers hidden behind selected pills after taking dose. As the sequence of hidden numbers cannot be predicted by patients, but are known by the system for each month of medication prescribed, the system offers high confidence that patients who respond correctly have indeed taken their medication.

• PLHIV with drug resistant TB should be managed by DR-TB center in consultation with ART centre. The treatment of HIV positive individual with MDR-TB is the same as for HIV negative patients. However treatment is more difficult and adverse events more common. Due to the increased frequency of adverse drug events, rigorous monitoring in this particular group of patients is required in order to ensure adherence to treatment, early identification and treatment of adverse events and reducing lost to follow up.

**Anti-retroviral therapy and co-trimoxazole prophylactic therapy in HIV infected TB patients:**

In addition to TB treatment, all HIV-infected TB patients must be provided access to care and support for HIV disease, including co-trimoxazole preventive therapy and antiretroviral therapy. ART reduces TB case fatality rates and the risk of recurrent TB. Co-trimoxaxole preventative therapy has been shown to reduce mortality among PLHIV by preventing opportunistic infections.

• **Anti-retroviral therapy** must be offered to all patients with HIV and TB as well as drug-resistant TB, irrespective of CD4 cell-count, as early as possible (after 2 weeks) following initiation of anti-TB treatment. Appropriate arrangements for access to anti-retroviral drugs should be made for patients. However, initiation of treatment for TB should not be delayed.
<table>
<thead>
<tr>
<th>Clinical staging</th>
<th>CD4 cell count (cells/mm3)</th>
<th>Timing of ART in relation to initiation of TB treatment</th>
<th>ART Recommendations</th>
</tr>
</thead>
</table>
| Start ART irrespective of any clinical stage | CD4 count of any value | • Start ATT first  
• Start ART as soon as TB treatment is tolerated (between 2 weeks and 2 months) | Start ART Regimen TLE for patients not on ART.  
For patients already on 1st line ART, ZLN, shift to ZLE & continue ZLE even after ATT is stopped. |

*Rationale for ART recommendation during TB treatment:*
In the absence of ART, TB therapy alone does not significantly increase the CD4 cell count. Nor does it significantly decrease the HIV viral load. Thus, CD4 counts measured during active TB are likely to reflect the actual level of immune suppression. The use of HAART in patients with TB can lead to a sustained reduction in the HIV viral load. It can also facilitate immunological reconstitution, and decrease AIDS-defining illness and mortality. This benefit is seen across different ranges of CD4 counts.

*The use of the standard 600mg/day dose of EFV is recommended for patients receiving EFV and Rifampicin.*

*In women of child-bearing age, the use of contraceptives should be ascertained because of drug reaction, as and when NNRTIs and Rifampicin are being used.*

*Special Attention to be paid for monitoring hepatotoxicity*

**Immune reconstitution inflammatory syndrome (IRIS)** may occur in up to one-third of patients who have been diagnosed with TB and who have started ART. It typically presents within three months of the initiation of ART but can occur as early as five days. Patients with TB-associated IRIS most commonly present with fever and worsening of pre-existing lymphadenopathy or respiratory disease. The symptoms are similar to the paradoxical reactions seen in immuno-competent patients on ATT, but occur more frequently. Most cases resolve without any intervention and ART can be safely continued. Serious reactions, such as tracheal compression caused by massive adenopathy or respiratory difficulty, may occur. Therapy may require the use of corticosteroids.
First Line ART for HIV-TB

<table>
<thead>
<tr>
<th>TENOFOVIR 300mg + LAMIVUDINE 300 mg + EFAVIRENZ 600 mg (FDC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen</td>
</tr>
</tbody>
</table>

Second Line ART for HIV-TB:
The following regimens are available under the National Programme currently for second line ART:

**Tenofovir + Lamivudine + PI (Atazanavir / ritonavir or Lopinavir / Ritonavir)**

**Zidovudine + Lamivudine+ PI (Atazanavir / ritonavir or Lopinavir / Ritonavir)**

**Stavudine+ Lamivudine + PI (Atazanavir / ritonavir or Lopinavir / Ritonavir)**

**Abacavir+ Lamivudine+ PI (Atazanavir / ritonavir or Lopinavir / Ritonavir)**

Rifampicin alters the metabolism of Protease Inhibitors, including Atazanavir and Ritonavir and reduces their effectiveness in standard doses

**Initiating ART (Anti-Retroviral Therapy) in patients with DR- TB**

- The use of ART in HIV infected patients with TB improves survival for both drug resistant and susceptible disease. However HIV infected MDR patients without the benefit of ART may experience mortality rates exceeding 90%. The likelihood of adverse effects could compromise the treatment of HIV or MDR TB if both treatments are started simultaneously. On the other hand undue delay in starting ART could result in significant risk of HIV related death amongst MDR patients.

- For patients who are already on ART at the time of DR-TB diagnosis be continued on ART when MDR-TB therapy is initiated. Occasionally, patients with HIV-related TB may experience a temporary exacerbation of symptoms, signs or radiographic manifestations of TB after beginning TB treatment. This paradoxical reaction occurs in HIV-infected patients with active TB and is thought to be a result of immune restitution due to the simultaneous administration of antiretroviral and tuberculosis medication (IRIS Syndrome).
Timing of referral to ART Centre
The following algorithm can be followed.

Scenario-2
HIV diagnosed among TB patients

TB Treatment not yet initiated

Refer to nearest ART centre for management of TB and HIV

TB Treatment initiated (intermittent regimen)

HIV Care & Support Services
Switch-over from RNTCP intermittent to RNTCP daily regimen

switch over from intermittent to daily regimen steps

ICTC

- Information on current TB treatment
- 10-point TB counselling tool
- Co-ordinate with RNTCP staff to make sure pt. carries copy of TB Tt card/c cardi to ART centre

ART Centre

- Receive pt., RNTCP documents, referral for Tt. Form on daily regimen
- Initiate Daily ATT

DMC/TU/DTC/STC

- Co-ordination of pt flow from ICTC to ART centre alongwith relevant documents
- Information sharing between ART Centre/TB unit/ DTC/STC

- Patients who are not yet on ART should be provided with a referral to the ART centre immediately on identification as an HIV-infected TB patient. However, these patients (especially microbiologically confirmed pulmonary TB) should be counselled to attend the ART centre after at-least 2 weeks of anti-TB treatment have been completed, so that the risk of TB transmission to others is lessened.
• TB treatment should never be delayed, but it should be stressed to the patient to attend the ART centre as soon as possible, without delay. Patients who are on ART from a source other than NACO should be referred to an NACO ART Centre if they are willing or to their existing ART providers with information on TB treatment initiation otherwise.

Process at ART Centre

1. In view of advanced clinical stage of HIV disease, HIV-infected TB patients are to be evaluated for ART on priority (Fast-tracked). HIV-infected TB patients should be prioritized for CD4 testing.

2. The ART Centre Staff Nurse are to record patients’ TB notification number and name of referring unit in the pre-ART register (along with ‘entry point code’) and ART- register.

3. The ART Centre Staff Nurses are to record the patient in the “ART Centre TB-HIV Register”, and include information on whether or not ART was initiated.

4. If the HIV-infected TB patient is initiated on ART, they would also continue their CPT from the ART Centre.

5. The ART Centre staffs are expected to provide feedback to the referring physician. In particular, the ART Centre staff should communicate when they have assumed responsibility for CPT provision, so that the PHI Medical Officer can know if CPT is to be discontinued from that source.

6. The daily anti-TB regimen will be dispensed from ART centre on monthly basis to the patient by ART centre pharmacist.

Provision of Co-trimoxazole Prophylaxis Therapy (CPT) to HIV-Infected TB patients:

• Co-trimoxazole is a fixed dose combination of sulfamethoxazole and trimethoprim; it is a broad spectrum antibiotic that targets a range of gram-positive and gram-negative organisms, fungi, and protozoa. Co-trimoxazole is given routinely for the prevention of opportunistic infections in HIV-infected persons; this strategy is called Co-trimoxazole prophylaxis therapy. CPT reduces morbidity and mortality of HIV-infected patients in general and HIV-infected TB patients in particular. Additional points to remember include:

  • Dose for prophylaxis for adults (> 14 years old) and > 30 kg body weight): 960 mg (800 mg sulfamethoxazole + 160 mg trimethoprim) daily.

  • For children and very low-weight adults (<30 kg), CPT for these patients is managed by ART centres as per separate protocol.

  • CPT is provided to patients in monthly pouches.

  • CPT is self-administered by the patient on a daily basis, and not under direct observation.

  • CPT can be taken alongside anti-tuberculosis treatment (ATT) and ART. Many patients who are eligible for ART would also have CPT continued at ART center.

  • Pregnant patients are also eligible, regardless of foetus gestational age.

  • Patients should have no history of a serious drug allergy to sulpha drugs or glucose-6 phosphate dehydrogenase (G6PD) deficiency.
**Isoniazid Preventive Therapy (IPT) For PLHIVs**

IPT is one of the 3 I's globally recommended for prevention of incident TB among HIV infected individuals. Isoniazid is the most effective bactericidal, anti-TB drug available at currently. While it protects against progression of latent TB infection to active disease i.e. reactivation, it also prevents TB reinfection post the exposure to an open case of TB. In 2011 the World Health Organization (WHO) issued specific recommendations regarding the use of IPT in its guidelines on "Intensified TB case finding and isoniazid preventive therapy for people living with HIV in resource constrained settings". The key recommendations included the following:

a) Adults and adolescents living with HIV should be screened for TB with a clinical algorithm and those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT. The guideline strongly recommend use of Isoniazid 300 mg once daily for 6 months, in adult and adolescents,

b) Children living with HIV who do not have poor weight gain, fever or current cough are unlikely to have active TB

c) Children living with HIV who have any one of above symptoms may have TB and should be evaluated for TB and other conditions. If evaluation shows no TB, such children should be offered IPT regardless of their age.

d) Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom-based screening, and have no contact with a TB case should receive six months of IPT (10 mg/kg/day) as part of a comprehensive package of HIV prevention and care services

e) All children living with HIV who have successfully completed treatment for TB disease should receive INH for an additional six months

f) Although IPT is more effective among Tuberculin Skin Test positive individuals (TST), it is not a requirement for initiating IPT intervention among the PLHIV considering difficulty in logistics and administration of the TST,

g) Providing IPT to people living with HIV does not increase risk of developing isoniazid (INH) resistant TB later. Therefore, concerns regarding development of INH resistance should not be a barrier to providing IPT

**Steps in Provision of Isoniazid Preventive Therapy (IPT):** The IPT provision involves following steps:

a) TB symptom screening at ART centre /Link ART-Plus and LinkART centres

b) Investigations for diagnosis of TB, if found symptomatic

c) If found Asymptomatic, assessment for the eligibility of Isoniazid Preventive therapy

d) If found eligible, initiation of IPT and Registration in IPT register maintained at the Nodal ART centre

e) Monthly collection of Isoniazid

f) Systematic recording and reporting

g) Continued TB symptom screening on each follow-up visits and reconsideration of IPT if symptoms develop

**Monthly collection of Isoniazid:** All eligible patients are to be initiated on IPT. The regimen prescribed are as below:

a) **Adult and Adolescent:** Isoniazid 300mg +Pyridoxine 50mg (Vitamin B6) per day for 6 months

b) **Children above 12 months:** Isoniazid 10mg/kg +Pyridoxine25 mg (Vitamin B6) per day for 6 months
The strategy for monthly collection of Isoniazid + Pyridoxine is as follows:

a) Patients on ART monthly collection from the ART centre, LAC-Plus or LAC along with monthly collection of the ART

b) Patients in pre-ART care visit the ART centre only once in six months. These patients may collect the monthly Isoniazid/ Pyridoxine packet from the designated stand-alone ICTC.

**Systematic recording and reporting**

All events in the cascade of IPT implementation including symptom screening at all contacts, IPT eligibility assessment, investigations, and the compliance with regimen are to be systematically recorded and reported.

**Mechanism of IPT implementation**

The ART centre counsellor, staff nurse is to perform TB symptom screening (SS) among all the PLHIV attending the ART centre. If the SS is found negative, an IPT card is initiated, if the patient is found to be SS positive, s/he is referred to the ART centre Medical Officer for further opinion and investigations to rule out active TB disease. The MO prescribes the investigations and refers the patient to the ART centre staff nurse for inclusion in the TB/HIV Line-List.

In rest of the patients, the MO undertakes assessment for eligibility of the patient for IPT and also completes the IPT card. He further stamps patient green book with either “On IPT” or IPT deferred stamp based on the situation. Also in patients found not suffering from TB after the investigations the MO undertakes the assessment as above.

All patients found to be eligible for IPT are referred to the pharmacist for collection of drugs. Concurrently the MO ensures that the Patients White Card and the IPT card are sent to the ART centre data manager so that the IPT register is updated. The data manager in turn updates the IPT register and Staff Nurse later prepares the monthly IPT report based on this register. This flow of patient and information is depicted pictorially in Figure as follows.

**Figure: Mechanism of IPT implementation**

- TB Symptoms Screening (SS)
  - ART centre Counsellors to perform symptom screening (SS)
  - If SS negative initiate IPT CARD, if SS Positive refer to MO for investigations
  - MO orders investigations and refers to ART staff nurse for recording in TB/HIV LineList

- IPT Assessment
  - MO assess IPT eligibility and complete IPT card for SS negative
  - He stamps patient green book with either “On IPT” / IPT deferred stamp
  - If no TB after investigation in “SS” positive patient MO completes assessment as above

- IPT Collection
  - All eligible patients go to pharmacist to collect IPT
  - Patient White Card + IPT card flows to data manager

- Recording and reporting
  - Data manager completes IPT register
  - Staff Nurse prepares monthly IPT report
TB and diabetes
As a consequence of urbanization as well as social and economic development, there has been a rapidly growing epidemic of Diabetes Mellitus (DM). India has second largest number of diabetic people in the world. As per recent estimates, there are around 66 million DM cases, with a further 77 million people having impaired glucose tolerance.

People with a weak immune system, as a result of chronic diseases such as diabetes, are at a higher risk of progressing from latent to active TB. Hence, people with diabetes have a 2-3 times higher risk of TB compared to people without diabetes.

- About 10% of TB cases globally are linked to diabetes.
- A large proportion of people with diabetes as well as TB is not diagnosed, or is diagnosed too late. Early detection can help improve care and control of both diseases.
- DM can lengthen the time to sputum culture conversion and theoretically this could lead to the development of drug resistance if a 4-drug regimen in the intensive phase of therapy is changed after 2 months to a 2-drug regimen in the presence of culture-positive TB.
- People with diabetes who are diagnosed with TB have a higher risk of death during TB treatment and a higher risk of TB relapse after completing treatment.
- DM is complicated by the presence of infectious diseases, including TB.
- It has been argued that good glycemic control in TB patients can improve treatment outcomes
- The precise biological mechanisms that result in this interaction between Diabetes and TB are still not clear. Epidemiological models have shown that DM accounts for 20% of smear-positive pulmonary TB and recent analyses have indicated that the increase in DM prevalence in India has been an important obstacle to reducing TB incidence in the country

National framework for joint TB- DM collaborative activities

The overall purpose is to articulate the national strategy for TB-Diabetes Mellitus Collaborative Activities between RNTCP and NPCDCS so as to ensure reduction of TB and Diabetes in India. Following strategy is proposed for collaboration between NPCDCS and RNTCP
1. Establishing joint planning and review committee for collaboration at National, State and District levels.
2. Establishment of service delivery protocols that address joint activities is as follows:
   a. Activities to improve diagnosis and management of Diabetes among TB patients:
      • Screening of all registered TB patients for DM
      • Ensuring DM management among TB patients
   b. Activities to improve diagnosis and management of TB among diabetic patients:
      • Intensified detection of active TB disease among DM patients
      • Ensuring TB infection control measures in health care settings where DM is managed
      • Ensuring TB treatment and management in comorbid patients

3. Joint monitoring and evaluation with standardized reporting shared between NPCDCS and RNTCP
4. Joint training of key programme and field staff in Diabetes/TB activities
5. Awareness and IEC activities
6. Operational research to strengthen implementation of DM/TB Collaborative Activities
Mechanisms for collaboration between RNTCP and NPCDCS
Mechanism for collaboration comprise at the National level, a National TB-DM Co-ordination Committee (NCC) of key officials from NPCDCS and CTD, experts from WHO, national institutes and civil society; at the Stated level, State Coordination Committee on TB-DM, chaired by MD National Health Mission and at the district level, District Coordination Committee (DCC) under the chairmanship of District Collector. States may create Coordination committee on TB-Comorbidities and sub-committees (TB-DM, TB-Tobacco, TB-Alcohol) etc under the SCC for ease of functioning. Alternatively states may start with a separate committee till the systems are set and later on can be merged with the “one” body. These committees will ensure smooth coordination and oversight the collaborative activities.

Screening Intervention and Diagnosis of Diabetes among TB patients
- All TB patients who have been diagnosed and registered under RNTCP will be referred for screening for Diabetes. Referral of TB patients for screening for DM and its recording & reporting is responsibility of the Peripheral Health Institutions (PHI) where TB treatment is initiated.
- The screening for DM will follow the guidelines stipulated by NPCDCS in India. Those guidelines stipulate that fasting blood glucose (FBG) be carried out using a finger prick and glucometer with cut-off thresholds in line with those recommended by the NPCDCS.
- Screening TB patients for DM should be conducted as early as possible after diagnosis of TB; but can be done at any time during the course of TB treatment. Because of the difficulties in getting TB patients to first come to the clinic in a fasting state, TB patients will be initially screened with a random blood glucose (RBG) using a glucometer. If the RBG is less than 140 mg/dl, this is a normal result and no further tests need be carried out. If the RBG is at or greater than 140 mg/dl, this might indicate an abnormal glucose state and there is a possibility of DM. The patient will be asked to return in a fasting state, and a fasting blood glucose (FBG) will be carried out. FBG value at or greater than 126 mg/dl indicates DM. The criteria for diagnosing Diabetes will be as follows.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Fasting Glucose (mg/dl)</th>
<th>2-hour Glucose (mg/dl)</th>
<th>Post-Load</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus</td>
<td>&gt;=126</td>
<td>&gt;=200</td>
<td></td>
</tr>
<tr>
<td>Impaired Glucose</td>
<td>&lt;110</td>
<td>140 to &lt;200</td>
<td></td>
</tr>
<tr>
<td>Impaired Glucose</td>
<td>&gt;=110 to &lt;126</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Criteria for suspected Diabetes case is reading of 140 mg/dl for Random Blood Glucose by glucostrip. The suspected case needs to undergo Fasting Blood Glucose test and Post Prandial tests to confirm diabetes.
- The blood glucose testing will be done by a person designated and trained for the purpose at every peripheral health institution (PHI). Though, this would vary from site to site the following general principles would apply. Wherever, NPCDCS is being implemented, the Auxiliary Nurse Midwife (ANM) has been trained to use glucometer and screen people for DM. In case this mechanism is not available, the laboratory technician working in the PHI will be trained to do the test. If a PHI does not have a laboratory technician, then either the staff Nurse or any other staff designated by the MO-PHI will be trained to do the test.
Linkage of TB patients with DM for Diabetes care and management -
All Diabetic TB patients should be linked for diabetic care. In the districts where NPCDCS is being implemented, TB patients with DM or with a FBG at or higher than 126 mg/dl will be referred to diabetes care using a referral form for definite diagnosis and management. A referral and feedback mechanism will be developed to enable timely exchange of information. Good cooperation and collaboration will need to be developed between the two sets of staff working in the different service areas.
- At districts where NPCDCS is not implemented, TB patients should be referred to the nearest healthcare facility for further diagnosis and management of TB-DM comorbidity.
- TB patients diagnosed with Diabetes should receive the same duration of TB treatment with daily regimen as non-Diabetic TB patients.

Screening and referral of Diabetic patients for TB
- Four-symptom complex screening for active TB in Diabetes patients is to be done. Screening is expected to be carried out every time the patient visits the DM clinic. Patients will be asked whether they are on TB treatment, and if not, they would be screened for four-symptom complex, i.e., Cough of any duration, Fever, Weight loss, Night sweat.
- The Screening results for Diabetics are to be recorded in the patient NPCDCS register
- NCD clinic will implement basic infection measures as stipulated in RNTCP guidelines

Linkage of Diabetic patients with TB for TB case management-
On screening, patients with one or more symptoms will be referred to nearest diagnostic facility for diagnosis of TB. A referral and feedback mechanism will be developed to enable timely exchange of information. The patients diagnosed for TB would be initiated on TB treatment as per management guidelines stipulated in RNTCP.

TB and nutrition
Under nutrition is considered as one of the risk factors in the development of TB, since under nutrition is known to adversely affect the immune system. Still, there remains a question as to whether malnutrition predisposes to tuberculosis, or whether it is a consequence of the disease. There is as yet little evidence showing that additional nutrition support improves TB-specific outcomes, but low body mass index as well as lack of adequate weight gain during TB treatment are associated with an increased risk of TB relapse and death.

The basic recommendations to address nutritional needs of TB patients are discussed below:
1. Conducting an initial nutrition assessment of TB patients with further monitoring;
2. Providing ongoing counselling for patients on their nutritional status; Diet for TB patients starting treatment should include: cereals (maize, rice, sorghum, millets, etc.); pulses (peas, beans, lentils, etc.); oil; sugar, salt; animal products (canned fish, beef and cheese, dried fish); and dried skimmed milk.
3. Management of severe acute malnutrition should be treated according to national guidelines and WHO recommendations;
4. Management of moderate under nutrition for TB patients who fail to regain normal Body Mass Index (BMI) after two months of TB treatment or appear to lose weight during TB treatment should be evaluated for a proper treatment adherence and other comorbidities. If indicated, these patients should be provided with locally available nutrient-rich or fortified supplementary foods. Special categories of TB patients such as:
   - Children who are less than 5 years of age should be managed as any other children with moderate under nutrition. Pregnant women with active TB, patients with MDR TB should be provided with locally available nutrient-rich or fortified supplementary foods.
• Micronutrient supplementation for all pregnant women as well as lactating women with active TB. These women should be provided with iron and folic acid and other vitamin and minerals to complement their maternal micronutrient needs. In situations when calcium intake is low, calcium supplementation is recommended as part of antenatal care.

The Guidelines on Nutritional assessment and supplementation for the TB patients in India are being prepared so that the programme can adapt the basic principles of nutrition for better outcomes.

Under nutrition and underlying food insecurity are among the most important determinants of TB. Improving nutritional status at population level is important for TB prevention. This should be part of broader actions on social determinants. All efforts should be made to link TB patients for the nutritional support. It can be through the existing public distribution system, local self-government or NGO or donor agencies or through corporate sector under Corporate Social Responsibility (CSR).

Management of severe acute malnutrition: Children below 5 years, School-age children and adolescents (5 to 19 years), and adults, including pregnant and lactating women, with active TB and severe acute malnutrition should be managed for severe acute malnutrition.

TB and tobacco

India is the second largest consumer and the third largest producer of tobacco in the world (FAO, 2005). Nearly one million Indians die from tobacco use every year, which is much more than combined mortality resulting from HIV/AIDS, TB and Malaria. As per Global Adult Tobacco Survey, (GATS 2010, a household survey of persons 15 years of age and above) there are 275 million adult tobacco users in India. It is estimated that more than one-third (35%) of adults in India use tobacco in some form or the other. The prevalence of smokeless tobacco use (26%) is almost twice that of the prevalence of smoking tobacco (14%).

Tobacco smoke contains toxic chemicals which cause disturbances in the bronchial surface of the lung. It also weakens the immunity of the patient to fight with the TB bacteria. The following evidence emerges from several studies conducted to look at the association of TB and tobacco in India:

• Almost 38% of TB deaths are associated with the use of tobacco.
• Prevalence of TB is 3 times as high among ever-smokers as compared to that of among never-smokers.
• Mortality from TB is 3 to 4 times as high among ever-smokers as compared to that among never-smokers.
• Smoking contributes to half the male deaths in 25-69 age groups from TB in India.

Exposure to tobacco smoke has also been found to affect TB in the following ways:

• Increase the risk of tuberculous infection and the risk of developing TB
• Affect clinical manifestations and increase risk of relapse among TB patients
• Affect microbiological conversion (sputum smear or culture) and outcome of treatment in TB patients
• Increase tuberculosis mortality and drug resistance to anti-tubercular drugs
Integrating Brief Advice for Tobacco Cessation

- When a patient gets registered as a tuberculosis case, the status of tobacco use is enquired.
- The information will be recorded in the TB treatment card in front portion using stamp
- If the TB patient is a smoker or tobacco user, he/she is offered 'Brief Advice' to quit tobacco used based on 5As and 5 Rs model
- The patient is assessed at every visit for follow up for TB and the status of tobacco use or quitting. At the end of treatment, his/her status of tobacco use is recorded in treatment card.
- If the patient has not quit tobacco use, he/she will be referred to the nearest Tobacco Cessation Clinic (TCC) or Quit line or m- cessation initiative.
- The information recorded in treatment card will be sent through the existing HMIS under RNTCP

Brief advice for quitting tobacco use consists of 5 'A's

1. **Ask** the patient if he/she is a tobacco user, during the course of every visit.
2. Briefly **Advise**against continuing tobacco use and link the current condition/ailment to continued tobacco use, where possible. Eg, “Quitting smoking/tobacco use would improve your health and will aid in early recovery from illness.”
3. Then **Assess** readiness to quit by asking the patient whether he or she is ready to quit tobacco use at this time. Eg, “How recently have you thought about quitting tobacco?” If the patient appears ready to change (quit), next steps are:
4. **Assist** the tobacco user in making a quit plan.
5. **Arrange** for follow-up by setting the next contact date.

If the tobacco user is not yet thinking about quitting tobacco use, the doctor/counsellor/treatment supporter will promote greater awareness of the **Relevance** to the patient of the advice to quit, the **Risks** of tobacco use and the **Rewards** (benefits) of quitting. Many tobacco users are largely unaware of the potential harm that continued tobacco use can do to them. If the patient is not ready to quit, the doctor/ counsellor/treatment supporter must not push the patient. People usually need time to change the mindset. If the patient is at least thinking about quitting, the doctor/ counsellor/treatment supporter can find out the patients’ **Roadblocks** to quitting and help the patient see ways to overcome these. This process will assist the patient to get ready for quitting the tobacco use, without being forceful.

The 5 R’s are :

- **Relevance** of quitting
- **Risks** of continuing
- **Rewards** of quitting
- **Roadblocks** to quitting
- **Repeat** at each visit

Awareness and IEC

- All the DOTS centre/Clinics will be made tobacco free
- IEC material will be displayed at TUs, DMCs and Tobacco Cessation Clinics.
- DMCs and TUs will display IEC material about the hazards of tobacco use, along with the brief advice.
- Tobacco Cessation Clinics will display hygiene and TB awareness related materials.
- Awareness building efforts will be done at both units for patients and staff.
- Sensitisation of all stakeholders (partners, policy-makers and administrators) will be done on regularly basis.
- Every effort will be made by both the programme divisions to sensitise the community about the ill effects of TB and tobacco use

**Recording & reporting**: Information on tobacco usage and its status is captured in treatment card.
Involvement of National Tobacco Control Programme in tuberculosis control

For enhancing active screening of TB patients through NTCP, the following process is indicated:

- Screening of four symptoms of active TB among tobacco users registered at the District TCC clinic and NCD Clinic at CHC - cough, fever, night sweat and weight loss
- Quit line established for tobacco cessation advice to conduct follow up of comorbid patients (TB patients with tobacco use) registered as TB cured, to identify TB relapse cases
- m-cessation initiatives to include TB-screening symptoms in cessation modules to identify active TB cases in people registered for tobacco cessation
- Ensure implementation of infection control guidelines in TCC Clinics
- Tobacco training modules prepared for teachers to include TB symptoms for increasing awareness among children and young adults

TB & Silicosis

Occupational high-risk group: Although reliable statistics are not available in India, it is known that thousands of workers and local residents are exposed to hazardous silica levels during stone crushing operations. Studies have shown increased morbidity and mortality rates among stone crushing mill workers from silicosis, lung cancer, and other lung diseases. Several other occupations also increase risk for tuberculosis including coal and other mining, tobacco (bidi rolling) and carpet weaving. Vulnerable and socially marginalised groups including tribal communities, children and migrant population are often used in these industries and do not have access to routine health services.

The RNTCP is in process of engaging with the Ministry of Labour and Mining to identify high priority districts with stone crushing units / mining industry. The specific guidelines will be developed to support persons with an occupational risk for TB and provide access, diagnosis and treatment services from the programme.
Human Resource Management

Most of the success that RNTCP has achieved can be attributed to its team of dedicated, hard-working and knowledgeable workers. Being under the overall umbrella of NHM, the HR policy and practice is mostly governed by the State NHM setup. The Central TB Division supplements this by provisioning contractual staff at strategic positions of the programme network, developing terms of reference for hiring of these staff and formulating standardized training material for creating a uniform knowledge base among workers. Apart from general health system staff, RNTCP has provisioned dedicated programme staff at various levels. The human resource structure given in next page enumerates key RNTCP positions at various levels.

Apart from these RNTCP positions, the States have been given the flexibility to create new structures and positions under their own health society mechanisms. Detailed terms of reference of these staff is provided at www.tbcindia.gov.in

Hiring of these staff is done by respective State/District Health Societies (other than National level positions). The compensation package for RNTCP contractual staff has to be decided by respective States, based on State specific situation, Job contents, Job responsibilities, and compensation for similar positions in other programmes under National Health Mission. Terms of reference of staff will be as per the programmatic guidelines.

RNTCP has adapted a cascading methodology to train its Staff, with National institutes and NRLs being involved as centres for training the trainers (STO, STDC Staff, IRL Staff, DTO, Medical College faculty, MO-STC -, etc.) on various components of the programme. These trainers come back and train the relevant cadre. The State TB Training and Demonstration Centres (STDCs) have been playing a major role in imparting State level RNTCP trainings. The MO-TCs and supervisory staff (STS, STLS) are trained at the STDCs who go on to train Treatment Supporters and lab technicians, respectively, at the district/Block/TB Unit level. DTOs with support of MO-TCs are entrusted with the responsibility of training the Medical Officers at district level.

The entire training process is reported under RNTCP programme management activities and closely monitored by National/State/District officials.
**Capacity building**
Capacity building is based on standardized modules which elaborate the technical and management components of the program. Special areas like pediatric TB, Drug resistant TB, TB with co-morbidities, Extra-pulmonary and other serious forms of TB, PPM, IPC, ACSM, SME etc are covered in these modules and also detailed as annexures to the main modules. Various categories of HR are trained/sensitized with the concise forms of these modules. The pharmacists, staff nurses, ANM, MPW, MPHS, Community volunteers are all trained with the same module for MPWs.
The customized modules for programme officials and staff, PPs, NGO functionaries, medical college faculties which include non-practicing TB teachers, non-practicing policy teachers, general practitioners, specialists, post graduates, researchers and professional associations are being developed using the advancement in ICT through capsular online e-training. The courses for each HR category ranging from the national policy makers and program managers to the community volunteers and patients’ peer group are compiled based on their TOR and Job Responsibilities with clear focus on development of necessary skills to perform the tasks for each type of trainee. The curriculum matrix thus designed is available on www.tbcindia.gov.in

**Training schedule**

**Induction training:** Initial training before assuming the responsibilities of the programme

**Update training:** Newer initiatives or changes in the policy of the programme are to be conveyed to the health personnel

**Re-training / refresher training:** Based on training needs of the identified personnel focused on specific deficits of knowledge or skills

For duration and content of training for each cadre the matrix of training courses (with defined content) is to be used for need based scheduling of training which is placed on www.tbcindia.gov.in under HRD section. The first step for planning of each training and retraining is periodic training needs assessment.
**Procurement & supply chain management**

An uninterrupted supply of good quality Anti TB Medicines is an essential component of DOTS strategy under RNTCP. Managing the supply chain in a programme requires continuous monitoring at all levels.

**Procurement**

**At Centre level** – Anti-TB drugs, Binocular microscopes, LED Fluorescence microscope, CBNAAT equipment, CBNAAT cartridges, LPA, Solid and Liquid culture lab equipment and consumables, PDA/Tablet computers, barcode printers and scanners

**At State / District level** – Laboratory consumables and equipment, computers, vehicles, printing materials, IEC materials, PPD vials, refrigerator, air conditioners etc.

For **1st Line treatment**, RNTCP has two regimens: treating new and retreatment cases. The medicines for patients are available as independent Patient-Wise Boxes (PWBs) containing medicines for the entire treatment of the patient.

For **2nd line treatment**, monthly Patient Wise Boxes (Type -A, Type-B & Type-C PWBs) for the different patient weight bands are made available by the programme.

Further, Cap Rifabutin-150mg is also procured centrally for co-infected TB HIV patients, put on 2nd line ART regimen. With regard to distribution, supplies of Cap Rifabutin are also delivered at GMSDs by manufacturers and are further distributed to RNTCP State Drug Stores, based on the NACO requirement. Upon receipt of Rifabutin supplies at SDS, they are further distributed to respective SACS (State AIDS Control Societies) based on their monthly stock reports.

Procurement of 1st Line Anti TB Medicines is limited to 'Prequalified Suppliers' defined as GMP compliant manufacturers as assessed by WHO Pre-qualification Programme (PQP) whereas 2nd Line Anti TB Medicines are procured from suppliers having WHO GMP certification as a requirement for the bidding process. For GFATM, procurement of 2nd line medicines is through Global Drug Facility (GDF) of Stop TB Partnership.

**LED / Binocular Microscopes** are also procured at the Central level by the Procurement Agency as per the General Finance Rules / World Bank procurement guidelines as funding for these is through Domestic Budget Support/World Bank credit.

**Supply Chain Management**

A good Supply Chain Management knows when to order or issue and how much to order or issue in order to maintain appropriate stock levels of all products to avoid stock outs and overstocking which can lead to product loss due to expiry. This is critical to the success of all health programs.

**Distribution:** The First Line Medicines are received at the GMSDs from the suppliers and based on the Monthly State Drug Stores and District Quarterly Programme Management and Logistics Report (QRPML), medicines are issued from the GMSDs.

For **2nd Line medicines**, loose medicines are supplied at the GMSDs/SDS which have to be repacked into 1-monthly Type A, B and C Boxes for all the different weight bands. These Monthly boxes are then labelled, taken into record and distributed by the SDS as per requirement of the districts. The DTC in turn sends these boxes based on the quarter reports to its implementing TU to the PHI and finally to the DOT Centre/Provider, as the case may be.
Monitoring of Anti-TB Medicines is done based on Monthly and Quarterly Programme Management & Logistics Reports from PHIs and TU & Districts respectively. The underlying presumption for consolidation of downline reports is that the QRPML should indicate accurate data on actual stock consumption and stock availability at all its downline medicine stores.
One of the important aspects of monitoring is Expiry Management wherein it is important that Principles of First-Expiry-First-Out (FEFO) are strictly adhered to by the drug stores at all levels to prevent expiry of medicines.

**Reconstitution of medicine boxes** is a process of retrieving residual medicines from PWBs of lost to follow up, dead and transferred-out patients and repacking them in quantities equivalent to and as per the description given on fresh PWBs for new & retreatment cases / Prolongation Pouches / loose medicines etc. It should be strictly centralized at the District Tuberculosis Center (DTC) or SDS for First line and Second Line medicines respectively.

**Quality Assurance** of Anti-TB Medicines has been accorded special importance by RNTCP and measures are taken at the time of procurement and also Post Procurement to maintain quality of Anti-TB Medicines. A comprehensive Quality Assurance (QA) Protocol is in place wherein samples from the field are regularly picked up for testing. This ensures continuous availability of good quality medicines at all stocking/ service delivery points under the programme.

**Standard Operating Procedures (SOP) and Training Manuals** have been developed for management of medicines. The SOP covers following aspects of supply chain management and provides detailed best practices to be followed by the State/ district/TU/PHI :-

- **Arrangement for transportation of Medicines** - States should enter into a contract with these transporters for dispatches from SDS to districts and downline destinations.
- **Physical Verification** of inventory of anti-TB medicines and reconciliation thereof with store records should be carried out under the supervision of the concerned officer-in-charge at the State, DTC, TU & PHI drug stores, regularly at the end of each month.
- **Communication Infrastructure / Staffing** at the medicine stores
- **Location, Space and Storage arrangements** should be adequately available as per Good Storage Practices (GSP).
- **MIS for Medicines stock management**

For details, refer to SOP for district drug store and State drug stores available at tbcindia.gov.in.

**Capacity building and Trainings** on the SOPs are regularly conducted by CTD at the central & state level, as part of decentralization of this key area.
Stocking Norms for 1st Line Anti TB Drugs :-

<table>
<thead>
<tr>
<th>Level</th>
<th>Stock for utilization</th>
<th>Reserve stock</th>
<th>Drug requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHI</td>
<td>1 month</td>
<td>1 month</td>
<td>(Monthly consumption x 2) – (existing stock in PHI at end of the month)</td>
</tr>
<tr>
<td>TU drugstore</td>
<td>0 months</td>
<td>2 months</td>
<td>(Quarterly consumption / 3) x 4 – (existing stock in TU including PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>DTC drugstore</td>
<td>0 month</td>
<td>3 months</td>
<td>(Quarterly consumption / 3) x 7 – (existing stock in DTC drug store including TU &amp; PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>SDS</td>
<td>0 months</td>
<td>3 months</td>
<td>(Quarterly consumption / 3) x 10 – (existing stock in SDS including stocks at all districts at end of the quarter)</td>
</tr>
</tbody>
</table>

Criteria for identification of short expiry Patient Wise Boxes (PWBs)

It is important that proactive measures be taken to ensure transfer of drugs to other districts/states to prevent expiry. The table below explains how to identify short-expiry drugs in the stores.

<table>
<thead>
<tr>
<th>Item</th>
<th>Duration of treatment</th>
<th>Extension in IP</th>
<th>Possible Interruption</th>
<th>Max transit time for shifting of box</th>
<th>At risk of expiry, if less than *</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC-1 PWB</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>PC-2 PWB</td>
<td>8</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

* At the district level
Stocking Norms for 2nd Line Anti TB Drugs

Flow of Drugs: At the beginning, the PHIs are supplied with a stock of two months (ie. stock for utilization in the first month along with a reserve stock of one month). Then every month, as per the monthly PHI report, they are supplied with stock from the TU which helps to maintain the reserve stock for a month at the PHI.

For the TU level to ensure that the PHIs have a month’s utilization stock plus a reserve stock for one month, it needs to have a reserve stock of two months at the beginning of the quarter. District drug stores to replenish the stock at TU, upon the receipt of the drugs from their respective State Drug Stores, as per the stocking norms.

The district drug store should have at least a utilization stock of 1 month at the beginning of the quarter. Similarly the State Drug Stores should have at least a reserve stock of 3 months of consumption of the state.

It is expected that buffer stocks shall also be ensured at each level as per the stocking norms given in the table below.

<table>
<thead>
<tr>
<th>Level</th>
<th>Stock for utilization</th>
<th>Reserve stock</th>
<th>Drug requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHI</td>
<td>1 month</td>
<td>1 month*</td>
<td>(Monthly consumption x 2) – (existing stock in PHI at end of the month)</td>
</tr>
<tr>
<td>TU drugstore</td>
<td>0 months</td>
<td>2 months</td>
<td>(Quarterly consumption / 3) x 4 – (existing stock in TU including PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>DTC drugstore</td>
<td>0 month</td>
<td>1 months</td>
<td>(Quarterly consumption / 3) x 5 – (existing stock in DTC drug store including TU &amp; PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>SDS</td>
<td>0 months</td>
<td>3 months</td>
<td>(Quarterly consumption / 3) x 8 – (existing stock in SDS including stocks at all districts at end of the quarter)</td>
</tr>
</tbody>
</table>

*All PHIs may not have a reserve stock. Only PHIs where patient/s are initiated or on treatment will have reserve stock of second line drugs.

With regard to substitution of Tab Levofloxacin (Type-A Box) with Tab Moxifloxacin for Levofloxacin resistant MDR patients and substitution of Inj. Kanamycin (Type-B Box) with Inj Capreomycin for Kanamycin resistant MDR patients, the same needs to be addressed and done at State Drug Stores only.
**Anti TB Drugs for adult patients in Daily Regimen**

The daily regimen is being initiated in five states and to be scaled up in other states in a phased manner.

Medicines for daily regimen are being supplied in Patient-wise Boxes (PWBs) in following weight bands:-

<table>
<thead>
<tr>
<th>Weight category</th>
<th>New TB Case</th>
<th>Previously Treated Case</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-39 kg</td>
<td>PC-1 DI</td>
<td>PC-2 DI</td>
</tr>
<tr>
<td>40-54 kg</td>
<td>PC-1 DII</td>
<td>PC-2 DII</td>
</tr>
<tr>
<td>55-69 kg</td>
<td>PC-1 DIII</td>
<td>PC-2 DIII</td>
</tr>
<tr>
<td>=70</td>
<td>PC-1 DIV</td>
<td>PC-2 DIV</td>
</tr>
</tbody>
</table>

Further, procurement of loose drugs for 5% of expected TB patients who may have side effects from fixed dose combinations (FDCs) and may require loose drugs instead of FDCs is also done through same mechanism and as per the procurement standards of GOI.

**Dosages:-**

<table>
<thead>
<tr>
<th>Type of TB Case</th>
<th>Doses in IP</th>
<th>Doses in CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>New</td>
<td>56 doses</td>
<td>112 doses</td>
</tr>
<tr>
<td></td>
<td>(7 days * 8 weeks)</td>
<td>(7 days * 16 weeks)</td>
</tr>
<tr>
<td>Previously treated</td>
<td>84 doses</td>
<td>140 doses</td>
</tr>
<tr>
<td></td>
<td>(7 days * 12 weeks)</td>
<td>(7 days * 20 weeks)</td>
</tr>
</tbody>
</table>

**Supply Chain Management**

- **Distribution and monitoring**: Drugs to be distributed in the same manner as it is being distributed under Intermittent Regimen.
- **Reconstitution of medicine boxes**: The reconstitution shall be done as per the existing RNTCP guidelines.
- **Treatment to Hospitalised patients** — preferably from the balance strips of PWBs from default / death patients. If same is not available, fresh boxes may be used.
- **Quality Assurance** of Anti-TB Medicines under daily regimen is same as it being done for Intermittent Regimen.
- **Storage**: Anti TB Drugs should be adequately maintained in quality condition; at room temperature, dry, pest / termite free area and secured under lock and key.
- **MIS for Medicines stock management** have been annexed at Annexures I-IV.
Stocking Norms for adult drug boxes:

For First three weight bands: 25-39 kg, 40-54 kg and 55-69 kg

Flow of Drugs: At the beginning, the PHIs are supplied with a stock of two months (i.e. stock for utilization in the first month along with a reserve stock of one month). Then every month, as per the monthly PHI report, they are supplied with stock from the TU which helps to maintain the reserve stock for a month at the PHI.

For the TU level to ensure that the PHIs have a month’s utilization stock plus a reserve stock for one month, it needs to have a reserve stock of two months at the beginning of the quarter.

The district drug store should have at least a utilization stock of 1 month at the beginning of the quarter. Similarly the State Drug Stores should have at least a reserve stock of 3 months of consumption of the state.

It is expected that buffer stocks shall also be ensured at each level as per the stocking norms given in the table below:

<table>
<thead>
<tr>
<th>Level</th>
<th>Stock for utilization</th>
<th>Reserve stock</th>
<th>Drug requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHI</td>
<td>1 month</td>
<td>1 month</td>
<td>(Monthly consumption x 2) – (existing stock in PHI at end of the month)</td>
</tr>
<tr>
<td>TU drugstore</td>
<td>0 months</td>
<td>2 months</td>
<td>(Quarterly consumption / 3) x 4 – (existing stock in TU including PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>DTC drugstore</td>
<td>0 month</td>
<td>1 months</td>
<td>(Quarterly consumption / 3) x 5 – (existing stock in DTC drug store including TU &amp; PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>SDS</td>
<td>0 months</td>
<td>3 months</td>
<td>(Quarterly consumption / 3) x 8 – (existing stock in SDS including stocks at all districts at end of the quarter)</td>
</tr>
</tbody>
</table>

*The stocking norms are different under daily regimen as the shelf life may be varied from 2-3 years.

For fourth weight band: >70 Kg

Flow of Drugs: Whenever a patient is diagnosed and to be put on treatment at PHI, the TU will send the drug box to the PHI immediately. At the end of each quarter, the shelf life would be reviewed and if required, inter TU or inter district transfers of the PWBs will be done to manage shelf life of drugs so that drug do not expired at any point of time. Accordingly, the stocking norms for the flow of drugs for weight band >70 are briefed in the table in next page:
<table>
<thead>
<tr>
<th>Level</th>
<th>Stock for utilization</th>
<th>Reserve stock</th>
<th>Drug requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHI</td>
<td>0 months *</td>
<td>0 months</td>
<td>Upon diagnosis of a patient under this category, respective TU will send the drug box to PHI immediately</td>
</tr>
<tr>
<td>TU drugstore</td>
<td>0 months</td>
<td>2 months</td>
<td>(Quarterly consumption / 3) x 2 – (existing stock in TU including PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>DTC drugstore</td>
<td>0 month</td>
<td>1 months</td>
<td>(Quarterly consumption / 3) x 3 – (existing stock in DTC drug store including TU &amp; PHI drug stores at end of the quarter)</td>
</tr>
<tr>
<td>SDS</td>
<td>0 months</td>
<td>3 months</td>
<td>(Quarterly consumption / 3) x 6 – (existing stock in SDS including stocks at all districts at end of the quarter)</td>
</tr>
</tbody>
</table>

Criteria for identification of short expiry Patient Wise Boxes (PWBs). The table below explains how to identify short-expiry drugs in the stores.

<table>
<thead>
<tr>
<th>Item</th>
<th>Months</th>
<th>Duration of treatment</th>
<th>Possible Interruption</th>
<th>Max transit time for shifting of box</th>
<th>At risk of expiry, if less than *</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC-1 D</td>
<td>6</td>
<td>2</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>PC-2 D</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

**TB HIV:** State Drug Stores will issue anti-TB drugs to the respective ART Centres as per the requirement quarterly. These ART centre shall submit the monthly report to the State Drugs Stores and the SDS to indicate the issues / dispatches to ART centres in their monthly report; submitted to the Central TB Division.
**Recording & Reporting**

Maintenance of accurate records and registers of patients and programme activities; and reporting data to the state/central unit, is essential for proper monitoring and management of Revised National Tuberculosis Control Programme (RNTCP). RNTCP records and reports are standardized and provide the required information for managing the programme effectively. The following standardized records are used in the RNTCP.

<table>
<thead>
<tr>
<th>Forms</th>
<th>Registers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Referral Slip</td>
<td>Tuberculosis Laboratory Register</td>
</tr>
<tr>
<td>Laboratory request Form for Specimen</td>
<td>Culture and DST Laboratory Register</td>
</tr>
<tr>
<td>Examination</td>
<td>Tuberculosis Notification Register</td>
</tr>
<tr>
<td>Tuberculosis Treatment Card</td>
<td>Second line TB treatment register</td>
</tr>
<tr>
<td>DR-TB Treatment Card</td>
<td>Stock Register</td>
</tr>
<tr>
<td>Patient’s TB Identity Card</td>
<td>Reconstitution Register</td>
</tr>
<tr>
<td>DR-TB patient identity card</td>
<td></td>
</tr>
<tr>
<td>Referral form for treatment</td>
<td></td>
</tr>
<tr>
<td>Referral form for treatment of DR-TB</td>
<td></td>
</tr>
<tr>
<td>Transfer Form</td>
<td></td>
</tr>
</tbody>
</table>

**RNTCP request form for examination of biological specimen for TB (Annexure 15A)**

The request form is kept at all the PHIs. It is filled generally by the MO of the referring health facility. This form is used for microscopy or CBNAAT or culture DST or Chest X-Ray or TST. Only one form is filled for each patient. Patient will report to the diagnostic health facility along with the request form. In case PHI is a sputum collection centre, sputum samples are sent to the diagnostic facility along with the request form. It is essential to record patient details, reason for testing and type of test requested. The same form is sent back to the treating unit with the results. When this format is used for C&DST, a copy of this form will be sent electronically to lab and DTC. In turn, the laboratory will send the result in electronic copy back to district with copy to DR-TB centre.

**RNTCP referral slip (Annexure 15B)**

The referral slips are used by peripheral health workers like ASHA, AWW, Link Workers etc. to refer patients to health facilities where specimen is collected either for examination or for transportation. This referral slip has contact details and symptoms of patient. At these health facilities, RNTCP request form for examination of biological specimen for TB is filled up by Medical Officer. (While printing Referral Slips, printing of Serial Number may be considered)

**Tuberculosis Treatment Card (Annexure 15C)**

Treatment card is filled at the PHI when patient is initiated on treatment. This card contains important information about a patient, such as: Name, age, sex and address of the patient; Type of disease; history of anti-TB treatment; Regimen prescribed; Duration of treatment; Amount of drugs to be given; Results of investigation before and during treatment; Drugs administered during the intensive and continuation phases of treatment; Treatment outcome of the patient; Retrieval actions for missing doses; Adverse event, Preventive treatment for children; details of X-ray or other tests for diagnosis of EP TB; information on TB comorbidity and Remarks. It also has information on the treatment supporter, person conducting the initial home visit and the signature of the MO. An additional treatment card should be kept, if treatment supporter is not at health facility. In such cases, treatment supporter should be trained on recording treatment card.
**Patient’s TB Identity Card** *(Annexure 15D)*

Identity card is completed for each patient who has a Tuberculosis Treatment Card. It is kept with the patient. Information from the Tuberculosis Treatment Card is used to complete the identity card. The front part of the ID card has patient information, name and address of the TU/ district and treatment details of patient including disease classification, type of patient, weight bands, smear results, category and information on the date of starting treatment. The back portion of the ID card has the results of follow-up smear examination, appointment dates for visits for drug administration and treatment outcome. This information will help to continue treatment in case the patient is transferred, or admitted to any other health facility anytime during the treatment period.

**RNTCP PMDT Treatment Card** *(Annexure 15E)*

This card is a key instrument for the treatment supporter administrating drugs daily to the patient. The card will be initiated at the DR-TB Centre when the patient is admitted for staring treatment. However for those patients who are not willing for admission the card will be initiated by the DTO. The card should be updated daily, ticking off the administration of drugs by the treatment supporter. The card is the source to complete and periodically update the PMDT register. The original treatment card will be maintained at the DR-TB Centre and a copy will be kept at treatment supporter. Accountable systems have to be developed locally for updating cards at all levels. When or if the patient moves from the DR-TB Centre to his/her district of residence a copy of the card, must follow the patient. A copy of this card may be used as a notification form and to inform about final outcome of treatment.

**RNTCP PMDT Patient Identity Card** *(Annexure 15F)*

When a patient is diagnosed as having DR-TB and is placed on a Regimen for DR TB, RNTCP PMDT patient identity card should be filled out by the health care provider at the same time that the treatment card is filled out. The card should be kept by the patient. The card, which is wallet-sized, contains the name, age, sex, PMDT TB number, essential information about the treatment (start date, regimen, and severe adverse reactions to drugs), and the details of the health centre and treatment supporter where the patient will receive treatment. Mention date of missed doses and date and result of all follow up cultures in the space under Intensive and Continuation Phase. It also has a place to write the date of the next appointment for follow up at DTC and the DR-TB Centre.

**Referral/Transfer form for treatment** *(Annexure 15G)*

Referral / Transfer form for treatment is kept at all health facilities. Medical officer of the diagnostic health facility which refers patients for treatment to other peripheral health facilities needs to fills in the top half of the form which includes the patient characteristics. Once the patient arrives, the receiving unit fills in the bottom half of the form, and sends it back to the referring unit. Information regarding referral of patient should also be noted in the TB notification register.

Referral / Transfer form is to be used when transferring registered patients on treatment from one reporting unit to another. If a patient is being ‘Transferred Out’, a Referral / Transfer Form and a copy of the Tuberculosis Treatment Card will be sent from the “transferring unit”, i.e., referring health facility / TU to the “receiving unit”, i.e., health facility/ TU where the patient will receive further treatment. The first part of the form contains information about the patient, her/his disease, treatment details and address of the transferring unit. This information should be used to complete a new Tuberculosis Treatment Card for the patient, who would be re-registered as a “transfer in” case in the receiving unit. When the patient has reported to the receiving unit, the bottom part of the form is completed by the receiving unit and returned to the transferring unit. It is to communicate patients’ follow up examination results at the end of intensive phase and treatment outcome to the transferring unit.
RNTCP PMDT Referral for Treatment Form (Annexure 15H)
This form has to be filled for all confirmed MDR or XDR TB cases that are referred from one centre to another centre. The form has to be filled by the doctor of the referring centre in duplicate and one copy sent along with the copy of the current treatment card to the referred centre. This form can be used for referring the patient at various points in time during the management of the patient between the PHI, DTC and DR-TB Centre for reasons like initiation of treatment, adverse drug reaction, transfer out, ambulatory treatment or any other reason. Incases that are transferred out, a copy of the updated PMDT treatment card must also be sent along with the referral for treatment form.

TB Notification register (Annexure 15I)
A TB notification register is maintained at each peripheral health facility. This register contains records of all patients diagnosed with TB and eligible for TB treatment, regardless of initiation of treatment. It will also incorporate those cases initiated on first line treatment and offered drug susceptibility testing and results are awaited. The registration data is based on the date on which a TB patient is diagnosed.

If patient is put on treatment in area of facility where s/he is diagnosed then information on treatment and follow up is recorded in the same TB notification register. If patient is treated in area other than where h/she is diagnosed then information on treatment and follow up is recorded in TB notification register of health facility where patients is residing.

In each health facility, TB notification register is maintained by its staff. STS of the respective TB units will support updation and coordination for completing the information.

For every patient, status of treatment should be recorded. The status of treatment for any patient would one of the following:
1. Initiated on First line treatment in the same Health Facility
2. Initiated on second line treatment in the same Health Facility
3. Initiated on treatment outside Health Facility
4. Treatment initiated outside RNTCP
5. Incomplete/ incorrect address
6. Died
7. Migrated & untraceable
8. Repeat diagnosis
9. Patient already on treatment/ Follow up patient
10. Wrong diagnosis
11. Referred for treatment with pending feedback
12. Other

RNTCP PMDT Treatment Register (Annexure 15J)
This register is maintained at DR-TB centre and at the district TB centre. In contrast to the TB notification register, it is restricted to patients who have actually started on a second-line TB treatment regimen. Date of registration will be date on which a patient is initiated on second-line treatment. The patients should be entered consecutively by their date of registration.

At DR-TB Centre, Medical Officer DR-TB centre will be responsible for maintaining the register. Statistical assistant will assist in updating it in consultation with districts and CDST laboratory. For patients who are unwilling for admission at the DR-TB Centre and are initiated on treatment at the DTC, the DTO will send the requisite information to the DR-TB Centre along with a copy of the treatment card. The DR-TB Centre will register the patient and communicate the PMDTTB number to the DTO electronically.
At district level, DR-TB supervisor will be responsible for maintaining and updating the register. In district level DR-TB register, every patient residing from the respective district and registered on treatment at DR-TB Centre will be registered using the PMDT TB number given from the concerned DR-TB Centre.

**Tuberculosis Laboratory Register (Annexure 15K)**

It is kept at all designated microscopy centres. The Tuberculosis Laboratory Register is used to record the results of smear examinations. The LT assigns a Laboratory Serial Number for each patient who has been referred to the Laboratory for microscopy. The TB laboratory register is used to record date of specimen collection, patient information including contact details, Name of the health facility that requested the examination (e.g. primary health centre, medical college, private practitioner, NGO, etc.); Reason for examination (diagnosis and follow-up); Results of smear examinations; information on testing for comorbidity and drug sensitivity and treatment initiation status and notification number. The last two columns of the register are for the LTs signature and any remarks the LT or supervisor wishes to make. The remarks column can mention in brief the action taken for patients belonging to other TU/districts, e.g., “Referred for treatment to…” The laboratory technician should summarize the information on sputum smear examinations done during that month. This information should be summarized in the format at the end of each month, printed in the Laboratory Register itself. Patients from the following month should be started from the next new page.

**Culture and DST Register (Annexure 15L)**

The RNTCP laboratory register for Culture and DST is used to record CBNAAT, LPA and culture and DST examination results. This register should be compared regularly with the RNTCP PMDT register to ensure that all DR-TB cases to be started on RNTCP Regimen for DR TB are entered in the PMDT register to ensure each case diagnosed is accounted for monitoring indicators and report generation. The lab NIKSHAY ID number is a unique number, given to a patient first time his/her specimen comes the lab. On all subsequent specimen sent to the lab, the same NIKSHAY ID number is retained for the patient, but the new specimen is provided with a new lab number. This gives an opportunity to easily extract the test results of all the specimen provided by the patient and there by track his/her response to the treatment.

**Stock Register**

This register is maintained at state/district/TU drug store. It is used for recording information on stock of drugs and consumables received and issued by the health unit. The register also mentions the batch numbers and date of expiry of drugs and consumables. The reconstituted PWBs should be recorded in the DTC stock register as receipts. The format of the register can be referred to in the Standard Operating Procedures Manual for State Drug Stores'.

**Reconstitution Register**

It is maintained at all the DTCs for recording the receipt of drugs of patients who have defaulted, died, failed treatment or transferred out. Such drug boxes are reconstituted and the details thereof are also recorded in the register. The format of the register can be referred to in the 'Standard Operating Procedures Manual for State Drug Stores'.