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.

Type of TB Case	Treatment regimen in IP	Treatment regimen CP
New	(2) HRZE	(4) HRE
Previously treated	(2) HRZES + (1) HRZE	(5) HRE

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.

Type of TB Case	Treatment regimen in IP	Treatment regimen CP
Rifampicin resistant + Isoniazid sensitive or unknown[2]	(6-9) Km LfxEto Cs Z E H	(18)LfxEto Cs E H
MDR TB[1]	(6-9) Km LfxEto Cs Z E *(Modify treatment based on the level of INH resistance as per the footnote)*	(18)LfxEto Cs E

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-Amoxyclav.

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.

Type of TB Case	Treatment regimen in IP	Treatment regimen CP
XDR	(6-12) Cm, PAS, Mfx, High dose- H, Cfz, Lzd, Amx/Clv	(18) PAS, Mfx, High dose-H, Cfz, Lzd, Amx/Clv

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.

Type of TB Case	Treatment regimen in IP	Treatment regimen CP
Rifampicin Sensitive INH Resistant[1] TB & DST of SEZ not known	(3-6) Km Lfx R E Z *(modify treatment based on baseline DST report to E,Z,KM, CM,Lfx, Mfx)*	(6) Lfx R E Z

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 Moxifloxacin, the sensitive one is to be used along with PAS and clofazimine.
- In case of resistance to both Levofloxacin and Moxifloxacin, 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.

Type of TB Case	Treatment regimen in IP	Treatment regimen CP
MDR or Rifampicin Resistant TB + Ethambutol resistance[1,2]	(6-9) Km Lfx Eto Cs Z	(18) Lfx Eto Cs
MDR or Rifampicin Resistant TB + Pyrazinamide resistance[1,2]	(6-9) Km Lfx Eto Cs E	(18) Lfx Eto Cs E
MDR or Rifampicin Resistant TB + Ethambutol + Pyrazinamide resistance[1,2]	(6-9) Km Lfx Eto Cs PAS	(18)Lfx Eto Cs PAS
MDR or Rifampicin Resistant TB + Levofloxacin	(6-9) Km Mfx Eto Cs Z E PAS Cfz	(18)Mfx Eto Cs E PAS Cfz
MDR or Rifampicin Resistant TB + Moxifloxacin	(6-9) Km Lfx Eto Cs Z E PAS Cfz	(18)Lfx Eto Cs E PAS Cfz
MDR or Rifampicin Resistant TB + Resistance to all Fluoroquinolones	(6-12) Km Eto Cs Z E PAS Cfz Lzd	(18) Eto Cs E PAS Cfz Lzd
MDR or Rifampicin Resistant TB + Resistance to Km only	(6-9) Cm Lfx Eto Cs Z E	(18)Lfx Eto Cs E
MDR or Rifampicin Resistant TB + Resistance to all SL Injectable	(6-12) Lfx Eto Cs Z E PAS Cfz Lzd	(18)Lvx Eto Cs E PAS Cfz Lzd

MDR-TB with mixed patterns of resistance

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

Type of TB Case	Treatment regimen in IP	Treatment regimen CP
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 SLIand 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 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-Amoxyclav, 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 hepatically 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

Weight category	Number of tablets (FDCs)		Inj. Streptomycin
	Intensive phase	Continuation phase	
	HRZE	HRE	
	75/150/400/275	75/150/275	gm
25-39 kg	2	2	0.5
40-54 kg	3	3	0.75
55-69 kg	4	4	1
>=70	5	5	1

**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

Weight category	Number of tablets (dispersible FDCs)			Inj. Streptomycin
	Intensive phase		Continuation phase	
	HRZ	E	HRE	
	50/75/150	100	50/75/100	mg
4-7 kg	1	1	1	100
8-11 kg	2	2	2	150
12-15 kg	3	3	3	200
16-24 kg	4	4	4	300
25-29 kg	3 + 1A*	3	3 + 1A*	400
30-39 kg	2 + 2A*	2	2 + 2A*	500

****A=Adult FDC (HRZE = 75/150/400/275; HRE = 75/150/275)***

Dosage for DR-TB for adults

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

**For mono-H resistant TB; [$]For Rifampicin Resistant TB*
[1]In 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)

Drug	Daily Doses*
Kanamycin / Capreomycin	15-30 mg/kg (SM 20-40 mg/kg)
Levofloxacin / Moxifloxacin	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

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

** 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:

History of treatment	Drug sensitivity status	Type of regimen
New	Drug sensitive or DST unknown / awaited	Regimen for new case
Previously treated	Drug sensitive or DST unknown* / awaited	Regimen for previously treated case
New or previously treated	Drug resistant	Regimen based on DST pattern

**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 Moxiflocaxin 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.