Appendix 18: Patient Information Booklet

Revised National Tuberculosis Control Programme
Central TB Division, Directorate General of Health Services
Ministry of Health & Family Welfare,
Nirman Bhawan, New Delhi

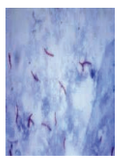
Patient Information Booklet on TB, Drug-resistant TB and Bedaquiline

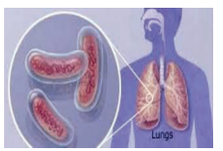
This guide is meant for MDR-TB patients to understand all you need to know about tuberculosis and MDR-TB. We hope this will help you clarify all your doubts and fears about this disease as well as enable you to cope with this illness, complete treatment as required and help you lead a healthy lifestyle during the treatment and thereafter.

TB is a curable disease and treatment is available free of cost. Yet in India we have 2.2 million cases of TB. MDR-TB has emerged as a public health problem. India is one of the countries with highest burden of MDR-TB. India accounts for 64 000 MDR-TB patients of the 300 000 MDR patients estimated in the world.

What causes tuberculosis?

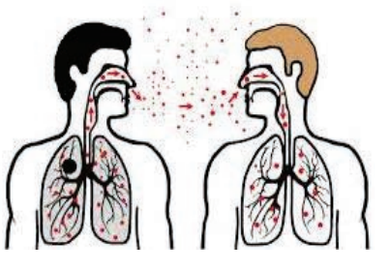
Tuberculosis (TB) is caused by bacteria (*Mycobacterium tuberculosis*) that most often affect the lungs.





How does it spread?

It spreads through the air when a person with TB (whose lungs are affected) coughs, sneezes, spits, laughs or talks.



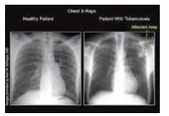
Symptoms of tuberculosis:

The symptoms of active TB include any of the following:

- *Cough for 2 weeks*
- *Fever for more than a month*
- *Blood in sputum anytime*
- *Loss of weight*
- *Loss of appetite*
- *Night sweats.*

Diagnosis of tuberculosis:

Tuberculosis is diagnosed by finding *Mycobacterium tuberculosis* bacteria in sputum which can be seen with the help of a microscope.

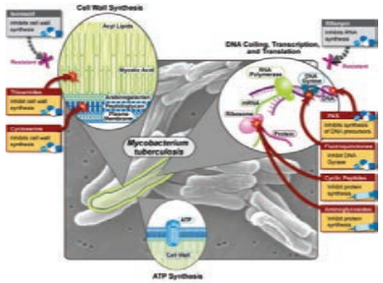


Tuberculosis treatment:

- Treatment is available is all government health facilities.
- Treatment is free of cost.
- Duration of treatment is as short as 6 to 8 months.
- Treatment has to be continued for the prescribed period.

What is multidrug-resistant TB?

- **Multidrug-resistant** tuberculosis (**MDR-TB)** is defined as a form of TB infection caused by bacteria that is resistant to treatment with at least two of the most powerful first-line anti-TB drugs, isoniazid (H) and rifampicin (R).



How does drug resistance develop?

- Use of inadequate regimen and inappropriate treatment adherence leads to increase in drug resistance levels in the community.
- MDR-TB is treated by second-line drugs. Incomplete and erratic treatment for MDR-TB leads to worsening of resistance and XDR-TB.
- All patients of MDR-TB cough out bacteria that are drug-resistant. These can infect another person with the same resistant bacteria. This is how MDR-TB spreads fast.

Who is at risk for getting MDR TB?

Drug-resistant TB is more common in people:

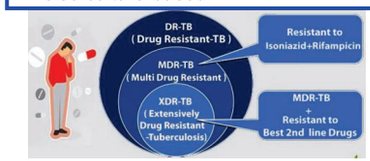
- who do not take their TB drugs regularly;
- who relapse with TB after being irregularly treated for TB in the past and are initiated on category 2 treatment of TB which is for 8 months;
- who are exposed to drug-resistant TB patients such as in families with an MDR patient;
- who are health workers working among MDR-TB patients;
- TB patients who are dependent on alcohol and habituated smokers and do not complete treatment.

Conditions to suspect MDR-TB:

- When people continue to have symptoms of TB even after 2 months of initiating treatment;
- Those TB patients who do not complete the full course of treatment;
- When a patient becomes sputum smear positive again after initial conversion at 2 months.
- Symptomatic contacts of an MDR TB patient

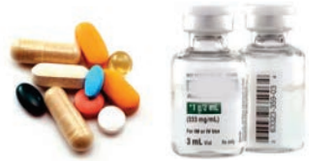
How to diagnose multidrug-resistant TB?

- Multidrug-resistant TB can be detected using special laboratory tests which test the bacteria for sensitivity to the drugs or detect resistance patterns.
- These tests can be molecular in type or else culture-based.



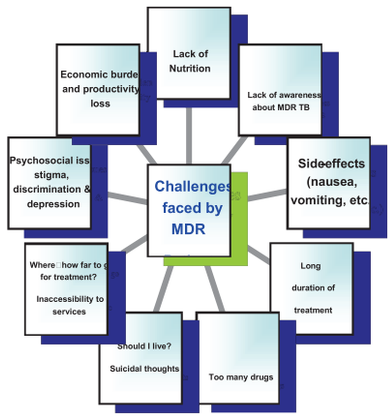
Management of MDR-TB:

- The total duration of treatment is about 24 months. This includes 6 months of injections and 6 drugs daily. The drugs are kanamycin, levofloxacin, ethionamide, cycloserine, ethambutol and pyrazinamide.



Challenges faced by MDR-TB patients:

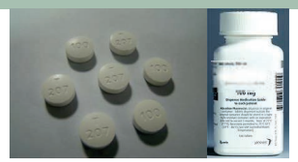
Treating MDR-TB is a challenging task, and there are challenges at every level.



Patients have to follow:

1. Patients must fully adhere to the treatment for TB
2. Family members of an MDR patient have to be investigated for TB
3. Children below 6 years of age in the same house of an MDR patient if negative for TB need to be initiated on drugs to prevent TB.
4. Patients have to take timely, affordable and nutritious food.
5. Patients have to avoid consumption of alcohol, smoking and other addictive substances
6. Patients have to follow preventive steps to avoid spreading the infection, such as covering the mouth while coughing.
7. Patients need to follow healthy lifestyle practices like exercise, yoga and positive thinking.
8. If a patient experiences any side-effects to the drugs, e.g. nausea, vomiting, giddiness, irritability, depression, nightmares, suicidal thoughts, etc. they should inform the doctor immediately. These side-effects can be managed and there is no need to panic or discontinue treatment.
9. The patient MUST complete the full course of 24 months of treatment and cannot afford to be irregular. The consequences of irregular treatment can be dangerous

INFORMATION ON BEDAQUILINE FOR PATIENTS



Some facts about this drug:

- The name of this drug is bedaquiline.
- It is in the form of tablet and is easy to swallow.
- This drug has shown promise in treating patients that are infected with the bacterium *Mycobacterium tuberculosis* especially for the drug-resistant TB variety.
- It might have potential value in combination with other anti-TB medications in the treatment of TB.

How do you take bedaquiline?

- It is in the form of a tablet and is easy to swallow.
- You will receive bedaquiline for 24 weeks (6 months) treatment of MDR-TB.

Take 400 mg (4 tablets) 1 time each day.

Take 200 mg (2 tablets) a day 3 times a week.

What are the possible side effects?

- Any drug can cause unwanted, unpleasant and sometimes harmful effects on the body.
- Drugs that are especially used for the treatment of MDR-TB are called second-line anti TB drugs.

The most common-side-effects are:

- Headache
- Common cold and sore throat
- Palpitation (feeling an irregular, fast or slow heartbeat)
- Heart rhythm may change (Qtc)
- Dizziness, fainting, lightheadedness
- Joint pain
- Nausea
- Vomiting

Benefits:

- There is a greater chance that you will be cured of tuberculosis
- You will possibly become better very much sooner than if you only took the standard medicines for treatment of resistant TB.
- Also, it is probably less likely that the drugs you are taking will develop resistance if you are taking bedaquiline.

What do I do when I have problems?

- You should tell your health-care provider immediately about any side-effect that you experience while taking bedaquiline.

What do women need to know?

All women must avoid getting pregnant while taking bedaquiline. If you are a woman able to become pregnant (i.e. not sterilized or less than 2 years since menopause), you should use 2 methods of birth control.

What do I do in case of pregnancy during treatment?

- Inform the health care provider immediately
- After evaluation in consultation with Obstetrician/ gynecologist you may be required to either terminate the pregnancy (MTP), get modified regimen without bedaquiline. You and the baby both may be evaluated for longer duration post treatment

What do men need to know?

- All men should avoid fathering a child while on treatment with bedaquiline. This is advised as the effects of the medication on your sperm are unknown; the effect of the medication also persists in the body for a period of many months.

What should I avoid while taking bedaquiline?

- You should not drink alcohol while taking bedaquiline.
- There are some medications that cannot be taken safety with bedaquiline.
- Make sure to inform your doctor if you are taking medicines or if medicines are recommended to you by a health-care practitioner for some other illness while you are on treatment for TB with bedaquiline.
- If you do not know the names of the medicines please ensure that you show the prescriptions to the TB doctor.

Can I take other medicines along with Bedaquiline?

- As there are many medicines that should be avoided with Bedaquiline for safety reasons, if any other medicine is required to be taken, it should be taken with permission from the concerned DR-TB Center doctor.

Drugs not be taken along with Bedaquiline

- Class 1a or Class III antiarrhythmic drugs (such as amiodarone, sotalol, procainamide, dysopyramide and quinidine)
- tricyclic antidepressants, including amitriptyline, doxepin, desipramine, imipramine, clomipramine
- the non-sedating antihistamines astemizole and terfenadine
- the neuroleptics-phenothiazines thioridazine, haloperidol, chlorpromazine, trifluoperazine, percycline, prochlorperazine, fluphenazine, sertindole, and pimozide
- the prokinetic cisapride
- Quinoline antimalarials (e.g., chloroquine and quinacrine)

Name & Contacts of DR-TB Center

_____

_____

_____

MDR-TB can be cured provided regular and uninterrupted treatment is taken by the patient

END THE GLOBAL TB EPIDEMIC

Let us all work together to overcome the scourge of MDR-TB

A WORLD FREE OF TB

Appendix 19: Patient Informed Consent Form

I am aware that I am suffering from a severe type of Tuberculosis (TB) which is resistant to some of the key drugs commonly used to treat multi-drug resistant TB (MDR-TB). This reduces my chances of getting cured if treated only with the standard regimen used for treating MDR-TB. I am therefore being offered the option of treatment with a new drug called Bedaquiline under the conditional access programme of the government along with other anti-TB drugs which are likely to improve my chances of getting cured.

I have been informed that there are known side effects that may cause discomfort to me and possible unknown side effects of the new drug Bedaquiline.

I understand that as part of this programme my clinical status will be monitored regularly and the information collected will be shared with relevant authorities where my personal information will be kept confidential.

I understand that my denial to consent won't be held against me and the best possible care available will be provided to me.

I understand that I am not eligible for any compensation in case of any adverse effect under this programme.

I declare that I am giving this consent under no influence or pressure in a conscious lucid state of mind of my own free will.

I have had the opportunity to ask questions about the programme and any question that I have asked has been answered to my satisfaction. I have been explained the patient education booklet in detail and a copy of it has been provided to me.

I give my consent voluntarily to take Bedaquiline having understood all the possible benefits and risks.

Patient's Name **Patient's Signature** **Date**

_____ _____ _____

*If the patient is unable to read and write or incapacitated / incompetent to make health care decisions, a surrogate decision maker must take the decision on behalf of the patient.

THUMB PRINT of Patient: ----------

Appendix 20: Cohort Event Monitoring Form

Sample treatment initiation form – CEM for TB drugs

Interview date: dd/mmm/yyyy

PATIENT DETAILS

Patient Name: ..... Patient ID: ……..…

Date of birth: dd/mmm/yyyy Age: ..... Sex at birth ❑ male ❑ female

TREATMENT PROVIDER

District Health Facility & address

Clinician/ Team Patient File number

Interview site ❑ Health Centre ❑ Hospital Clinic ❑ Phone interview ❑ Home visit ❑ Other

MEDICAL DETAILS

Weight (kg) Height (cm)

Indication for treatment ❑ Pulmonary TB ❑ Extra-pulmonary TB ❑ TB site/s:…… ❑ MDR-TB ❑ Prophylaxis

Prior exposure to anti-TB medicines ❑ No ❑ Yes ❑ Unknown

Pregnant ❑ Yes Date of LMP: dd/mmm/yyyy or estimated current gestation (weeks):

❑ Uncertain If PREGNANT record patient details in PREGNANCY REGISTER for follow-up

❑ No

Breastfeeding an infant ❑ No ❑ Yes

Injecting Drug Use Within Past Year ❑ No ❑ Yes ❑ Unknown

Tobacco use within the past year ❑ No ❑ Yes ❑ Unknown

Excessive alcohol use in the past year ❑ No ❑ Yes ❑ Unknown

Documented HIV infection ❑ No ❑ Yes ❑ Unknown

CURRENT AND PAST MEDICAL CONDITIONS & EVENTS (List)	Date of Onset	Date of recovery	Continues
			❑
			❑
			❑
			❑
			❑
			❑
			❑
			❑
			❑

LABORATORY & OTHER TESTS. Include laboratory tests taken at any time during the PAST 30 DAYS

Test	Date	Result (units)	Test	Date	Result (units)
Sputum smear			ESR		
Sputum culture			Total WBC		
Drug susceptibility*			Haemoglobin		
Line probe assay			ALT (SGPT)		
Nucleic acid testing			AST (SGOT)		
Tuberculin Test			Creatinine		
HIV Antibody			Creatinine Clearance		
CD4 Count			Glucose		
Chest X Ray		Cavities (Y/N)	Thyroid function (TSH)		
Audiometry			Electrocardiogram		QTc
Visual acuity			Other		
Hepatitis markers			Other		

MEDICINES							
Medicines & traditional medicines taken at any time in PAST 30 DAYS	Indication	Dosage	Frequency	Route	Start date	Stop date	Continues
							❑
							❑
							❑
							❑
							❑
							❑
							❑
							❑

* DST to the following drugs may be useful to record on this form or elsewhere in an accessible electronic medical record: isoniazid, rifampicin, kanamycin (and/or amikacin), capreomycin, ofloxacin (or ciprofloxacin), levofloxacin and moxifloxacin

All NEW Anti-TB medicines prescribed at this interview	Indication	Dosage	Frequency	Route	Start date	Anticipated Stop date
All other NEW medicines prescribed at this interview	**Indication**	**Dosage**	**Frequency**	**Route**	**Start date**	**Anticipated Stop date**

Name of the Reporter: .....

Please give this form to the CEM Focal Person

Focal Person: ..... Phone: .....

Date of next appointment: dd/mmm/yyyy

Instructions for the completion of the TREATMENT INITIATION FORM

A **Treatment Initiation Form** should be completed at treatment initiation: the interview at which anti-tuberculosis therapy is commenced and at which the patient is enrolled in the Cohort Event Monitoring programme. This form represents a template and the programme may wish to adapt it according to its needs and preferences; it includes all of the essential data elements to be collected for the CEM of TB drugs as recommended by WHO.

Patient participation

It is important that monitoring begins at the commencement of therapy. Patients may be enrolled if they are beginning treatment with the monitored medicine(s) for the first time (i.e. treatment naïve) or if their regimen is being changed. Patients who have previously been exposed to anti-TB medicines may also be included in the cohort, but monitoring should begin at the commencement of a new course of treatment.

Patients should be informed about the purpose of the monitoring programme and their agreement to participate should be sought prior to enrolment. Patients who are unwilling to participate should not be enrolled in the monitoring programme.

Patient ID

Type of identification to be selected by country.

Tick boxes (✔)

Where there are tick boxes, please answer by placing a tick ✔ in the appropriate box.

Patient details

Patient initials

Please use initials of given name(s) and family name.

Date of birth

If DOB is unknown, record the patient's age (or estimated age, if true age is unknown).

Treatment provider

Patient file number

Record the file number used to identify the patient in your clinic.

Medical details

Weight & height

Record the patient's current weight and height on the date of interview.

Pregnant

If this patient is currently pregnant, please record her details in the **Pregnancy Register** to ensure outcome of pregnancy is followed up.

Indication for treatment

Please indicate whether the anti-tuberculosis therapy is to be used for the treatment of pulmonary TB, extra-pulmonary TB, MDR-TB or for prophylaxis. More than one box may be ticked.

CURRENT AND PAST MEDICAL CONDITIONS & EVENTS (List)

Indicate any significant concomitant diagnoses, past medical conditions and events. Include the onset date, if known, and either record the date of recovery or, if the condition is ongoing, note that it 'continues' (Record the approximate date if the exact date is unknown).

LABORATORY & OTHER TESTS

Record the results (including *units*) of any laboratory tests taken in the PAST 30 DAYS. Commonly performed tests have been listed; other tests may be recorded in the space provided. The list of tests is indicative but may be reduced or increased depending on the regimen used and resources.

MEDICINES

Medicines & traditional medicines taken at any time in PAST 30 DAYS

Record the details of any prescription or over-the counter medicines and any traditional medicines, herbal remedies or health supplements taken at any time during the PAST 30 DAYS. Include the *units* the '**Dosage**' column. If a medicine is given as a fixed dose combination (FDC), either as a co-formulation or in a co-blister pack, record the number of dosage forms (DF) given.

All new medicines prescribed at this interview

Please record the details of all medicines prescribed at this interview, for TB or non-TB in the separate Tables.

Sample treatment review form – CEM for TB drugs

Interview date: dd/mmm/yyyy

PATIENT DETAILS

Patient Name: ..... Patient ID: ……..…

Date of birth: dd/mmm/yyyy Age: ..... Sex at birth ❑ male ❑ female

TREATMENT PROVIDER

District Health Facility & address

Clinician/ Team Patient File number

Interview site ❑ Health Centre ❑ Hospital Clinic ❑ Phone interview ❑ Home visit ❑ Other

MEDICAL DETAILS

Weight (kg) Height (cm)

Indication for treatment ❑ Pulmonary TB ❑ Extra-pulmonary TB ❑ TB site/s:…… ❑ MDR-TB ❑ Prophylaxis

Prior exposure to anti-TB medicines ❑ No ❑ Yes ❑ Unknown

Pregnant ❑ Yes Date of LMP: dd/mmm/yyyy *or* estimated current gestation (weeks):

❑ Uncertain If PREGNANT record patient details in PREGNANCY REGISTER for follow-up

❑ No

Breastfeeding an infant ❑ No ❑ Yes

Events	AE MedDRA/ WHO-ART code*	Record all NEW events or CHANGES in pre-existing conditions since last interview								
		Date of onset	Date resolved	Outcome*	Severity†	Seriousness‡	Rechallenge §	Causality¥ (for BDQ)	Expectedness ¢	Causality¥ for other drugs (with name)

OUTCOME*
- R1 Recovered/ resolved
- R2 Recovering/resolving
- S Recovered with sequelae
- N Not recovered/not resolved
- D Died
- U Unknown

MAXIMAL SEVERITY†
- 1 Mild
- 2 Moderate
- 3 Severe

SERIOUSNESS‡
- N Not serious
- H Hospitalization (caused or prolonged)
- P Permanent disability
- C Congenital abnormality
- L Life threatening
- D Death

RECHALLENGE§
- 1 No rechallenge
- 2 Recurrence of event
- 3 No recurrence
- 4 Result unknown

Scale used for grading of severity of AEs :

❑ Clinician's judgement ❑ CTCAE grading system ❑ DAIDS AE Grading Table

❑ Other (specify): .....)

* to be completed by PV centre after data collection (see also Instructions for completion)

CAUSALITY¥
1. **Definite**
2. **Probable**
3. **Possible**
4. **Unlikely**
5. **Unrelated**

EXPECTEDNESS¢:
- **E Expected**
- **U Unexpected**

LABORATORY & OTHER TESTS

Test	Date	Result (units)	Test	Date	Result (units)
HIV Antibody			ALT (SGPT)		
CD4 Count			AST (SGOT)		
ESR			Lactic acid		
Total WBC			Lipase		
Haemoglobin			Chest X-Ray		Cavities (Y/N)
Creatinine			ECG		QTc
Creatinine Clearance			Audiometry		
Glucose			Visual acuity		
Hepatitis markers			Other		
TSH			Other		

MEDICINES

Anti-TB medicines taken since last interview	Dosage	Frequency	Route	Start date	Stop date	Continues	Reason(s) for stopping #	Action**
						❑		
						❑		
						❑		
						❑		
						❑		
						❑		

Other medicines & traditional medicines taken since last interview	Dosage	Frequency	Route	Start date	Stop date	Continues	Reason(s) for stopping #	Action**
						❑		
						❑		
						❑		
						❑		
						❑		
						❑		
						❑		

REASON FOR STOPPING

1 Adverse event
2 Poor adherence
3 Course completed or cured*
4 Planned interruption
5 Planned medication change
6 No longer needed
7 Treatment failure*
8 Pregnancy
9 Drug out of stock
10 Cost
11 Patient decision
12 Died*
13 Lost to follow-up*
14 Other (please specify)

**ACTION TAKEN BY CLINICIAN IN CASE OF SUSPECTED ADVERSE EVENT LINKED TO A DRUG
Dose not changed
Drug withdrawn
Not applicable
Dose reduced
Drug interrupted

All NEW medicines (anti-TB & other) prescribed at this interview	Dosage	Frequency	Route	Start date	Expected stop date	Indication

Outcome* (to be completed at the end of current treatment episode)

❑ Cured	❑ Completed	❑ Treatment failed	❑ Died	❑ Loss to follow up	❑ Not evaluated

If the end of the treatment episode, treatment outcome date : dd/mmm/yyyy

* as per *Definitions and reporting framework for tuberculosis – 2013 revision (WHO/HTM/TB/2013.2). Geneva, World Health Organization; 2013. Available from: www.who.int/iris/bitstream/10665/79199/1/9789241505345_eng.pdf*

Name of the Reporter: .....

Please give this form to the CEM Focal Person

Focal Person: ..... Phone: .....

Date of next appointment: dd/mmm/yyyy

Instructions for the completion of the TREATMENT REVIEW FORM

A **Treatment Review Form** should be completed each time the patient is interviewed following commencement of treatment with the monitored medicine(s). This form represents a template and the programme may wish to adapt it according to its needs and preferences; it includes all of the essential data elements to be collected for the CEM of TB drugs as recommended by WHO.

Patient ID

Type of unique patient identification to be selected by country.

Tick boxes (✔)

Where there are tick boxes, please answer by placing a tick ✔ in the appropriate box.

PATIENT DETAILS

Patient initials

Please use initials of given name(s) and family name.

Date of birth

If DOB is unknown, record the patient's age (or estimated age, if true age is unknown)

TREATMENT PROVIDER

Patient file number

Record the file number used to identify this patient in your clinic

MEDICAL DETAILS

Weight & height

Record the patient's current weight on the date of follow-up visit. Height should be recorded for children at treatment review, but is unnecessary for adults.

Indication for treatment

Please indicate whether the anti-tuberculosis therapy is to be used for the treatment of pulmonary TB, extra-pulmonary TB, MDR TB or for prophylaxis. More than one box may be ticked.

Pregnant

Please indicate whether the patient is pregnant, uncertain or not pregnant. Women who are pregnant should be entered into a pregnancy register to ensure that the outcome of the pregnancy is followed-up.

EVENTS

Please record:

All **new health events** that have occurred since the patient started the monitored medicine. Include any **deterioration or improvement in pre-existing conditions** (or previously recorded events).

For each event, select the appropriate code for **Outcome**, **Severity**, **Seriousness** and **Rechallenge** from the shaded panel. Choose Clinician's judgement if no scale is used to classify the severity of the event other than the health professional's opinion. If the severity coding used is not "Mild", "Moderate", "Severe" please adjust accordingly. Indicate the "Scale used for grading of severity of AEs".

Coding of the events (using AE MedDRA or WHO-ART code) is done by the expert in pharmacovigilance in consultation with the clinician in charge of the patient; it is not necessarily performed by the person completing the questionnaire. A record on the attribution of an event to one or more medications will be made in the database but is not included in the forms.

LABORATORY & OTHER TESTS

Record the results (including *units*) of any laboratory tests taken since the patient was last interviewed. Commonly performed tests have been listed; other tests may be recorded in the space provided. The list of tests is indicative but may be reduced or increased depending on the regimen used and resources.

MEDICINES

Anti-tuberculosis medicines or regimen taken since last interview
Anti-tuberculosis medicines may be recorded either as individual medicines or as fixed dose combinations (FDC). Include start and stop dates for medicines that were started or stopped during the interval since the patient was last interviewed and indicate which medicines continue to be taken (continues ✔). For medicines that have been stopped, please select the **reason(s) for stopping** from the list of codes provided (more than one code may be used). For Anti-tuberculosis medicines, please also select the appropriate **adherence code**. Note: If a medicine was stopped and later restarted, include separate entries for each course. If the dose was changed, record the medicine again on a new line with the new dose and dates.

Other medicines & traditional medicines taken since last interview
Record the details of other medicines, including over-the-counter medicines and any traditional medicines, herbal remedies or health supplements taken since the last interview.

All new medicines (Anti-tuberculosis & other) prescribed at this interview
Record the details of all new medicines (Anti-tuberculosis and other medicines) prescribed at this interview.