



# Monitoring & Case Management

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Careful monitoring of drug-resistant TB patients, using a case management approach, is a critical component of effective TB control.

## Case management of drug-resistant TB

### Case management is:

“A collaborative process that assesses, plans, implements, coordinates, monitors, and evaluates the options and services required to meet the client’s health and human service needs. It is characterized by advocacy, communication, and resource management and promotes quality and cost-effective interventions and outcomes.”  
—*Commission for Case Manager Certification*

The goal of tuberculosis (TB) case management is to provide patient-centered care for completion of treatment, and to ensure all public health activities related to stopping transmission are completed.

Public health departments (i.e., under TB or communicable disease control programs) are encouraged to assign a specific health department employee (case manager) the primary responsibility for ensuring the patient is educated about drug-resistant TB, that therapy is continuous, and that contacts are examined. Some specific responsibilities may be assigned to other persons.

## Roles and responsibilities

Providing care for patients with drug-resistant TB is a team effort and a variety of staff and community members may be involved. It is very important that roles and responsibilities are clearly delineated and understood and that effective lines of communications are maintained. Duties and responsibilities may change throughout care as the patient’s needs change.

### Case manager

The case manager coordinates the care provided by the treating clinician(s), specialists, and other caregivers such as outreach workers, directly observed therapy (DOT) workers, social workers, correctional facility nurses, school nurses, and contact investigators. The case manager has primary responsibility for:

- Establishing a trusting relationship with the patient.

- Educating the patient and significant others about drug-resistant TB and its treatment.
- Developing an individualized case management plan.
- Ensuring the patient adheres to and completes treatment via DOT.
- Ensuring patient referral to appropriate supportive services.
- Ensuring individuals in contact with the patient are identified, located, prioritized, evaluated, and treated as needed.
- Ensuring response to therapy is evaluated regularly. If response is not in accordance with expected outcomes, ensure the treating clinician is informed.
- Monitoring for adverse effects of treatment and notifying the treating clinician if present.

Depending on the expertise, resources, and infrastructure of the clinic or medical provider managing the actual care of the patient, the case manager may have other roles and responsibilities. When primary clinical care is obtained through a private provider or when patients are hospitalized or incarcerated, the case manager may take on the role of liaison or coordinator-of-care. In addition to the previously listed responsibilities, the case manager:

- Facilitates exchange of information between the family, medical providers, laboratories, pharmacies, insurance companies, and the public health infrastructure.
- Builds relationships within all these systems to achieve the best results for the patient.
- Ensures expert consultation has been sought and provides referral for consultation as needed.
- Offers training, education, and resources to staff who will be providing patient care.

## Treating clinician

The treating clinician provides the direct medical care of the patient. Given the toxicities of the second-line drugs and importance of ensuring response to treatment, it is recommended that the treating clinician evaluates the multidrug-resistant (MDR)-TB patient regularly. See section: **Monitoring treatment response.**

When the treating clinician is not part of the public health team (e.g., private or community practice), it is essential to establish linkage with the public health department for case reporting, case management, and provision of DOT.

## DOT worker

The role of the DOT worker for patients with drug-resistant TB is similar to that for patients with pan-susceptible TB. However, because of the large number of pills needed and toxicity of second-line drugs, the DOT worker will need additional training to become familiar with expected side effects and strategies to support the patient in taking medications. In general, the DOT worker is responsible for:

- Watching the patient take pills
- Checking for side effects
- Protecting confidentiality

- Documenting the visit
- Communicating with the case manager and prescribing clinician regularly and immediately about symptoms of serious side effects
- Other duties, including helping patients keep appointments, providing education and offering incentives and enablers

The DOT worker may be the first person to identify a change in a patient's condition or development of an adverse reaction. DOT providers often develop strong relationships with MDR-TB patients because they see them daily and provide ongoing encouragement and support.

### Clinic staff

Nurses and other personnel at the TB or outpatient clinic may be involved with providing DOT, intramuscular (IM) injections, and assessments, as well as alerting the case manager and treating clinician about symptoms of serious side effects.

### Other staff

Other health department staff such as contact investigators, social workers, and community health workers may have important roles in the management and support of drug-resistant TB patients. This would include alerting the case manager and/or treating clinician about symptoms of side effects the patient may be experiencing. Additionally, staff in other organizations or outside the health department may have a role in supporting and/or treating the patient during treatment.

## Initiating treatment

### Initial evaluation

The important task of case managing and monitoring the patient with drug-resistant TB begins with a thorough and organized initial evaluation. The objective of the initial evaluation is to identify those patients at greater risk of adverse effects and to establish a baseline for monitoring.

### Medical history and physical evaluation

- Demographic information (name, address, date of birth, race and ethnicity, etc.)
- Past medical history (including allergies, HIV status or other immunocompromising conditions, diabetes mellitus, hypertension, acute or chronic renal insufficiency, acute or chronic liver disease, psychiatric history, thyroid disease, drug or alcohol dependence, pregnancy, chronic epilepsy or seizure disorder, and other complicating conditions as well as medication taken for these conditions)
- Full TB history including previous treatment (anti-TB medications, duration and dates taken, as well as location where treatment was given), TB symptoms and date of onset, surgeries, and complications; it may be helpful to document prior drug treatment in **Tool 1: Drug-O-Gram**
- Social history including: country of birth, lifestyle and habits, local family and social support network, employment, housing history, travel, as well as history of substance use, migration and incarceration

- Review of systems
- Focused physical exam
- Weight and height to assess nutritional status and calculate body mass index (BMI) and lean body weight
- Source case and contact information including incarceration history, previous residences, household contacts, and visitors

## Baseline examinations

- **Laboratory exams** should include HIV test, CBC, TSH, pregnancy test for women of childbearing age, and a comprehensive metabolic panel (obtain 24-hour creatinine clearance for any elevation of creatinine or question of renal insufficiency). **Tool 4: Laboratory Flow Sheet** may be helpful in summarizing bloodwork results that will be assessed at baseline and throughout treatment.
- **Hearing, vision** (acuity and color), **and vestibular function** should be assessed at baseline and results documented. **Tool 5: Vision Screening Flow Sheet** and **Tool 6: Hearing and Vestibular Flow Sheet** may be helpful for tracking these serial monitoring results.
- **Radiography** should be obtained prior to treatment initiation. Posteroanterior (PA) views (and lateral in children) of the chest for pulmonary disease are recommended. Additional views and/or CT scan may be helpful in some instances.
- **Sputum for nucleic acid amplification test (NAAT), acid-fast bacilli (AFB) smear, culture and drug-susceptibility testing (DST):** At the start of treatment, obtain 3 sputa for AFB smear and culture. Note: In a patient started on a standard TB regimen (RIPE) for 4 weeks or more prior to starting an MDR-TB regimen and for whom the initial isolate was not known to be resistant to **all** first-line drugs at baseline, request a repeat DST from a subsequent positive TB culture obtained near the time of MDR-TB regimen initiation. This will help to ensure that no additional resistance developed during the initial period of therapy. **Tool 3: Bacteriology Flow Sheet** may be helpful for summarizing the important microbiology, molecular tests, and DST results.
- **Rapid molecular assays for identification of drug resistance.** If not already obtained (and conventional DST results are still pending), all patients in whom a clinical suspicion for drug-resistant active pulmonary TB exists should have a sputum specimen submitted for Xpert MTB/RIF or other NAAT that evaluates for rifampin (RIF) and/or isoniazid (INH) resistance.
- **EKG:** For patients who will be taking bedaquiline (BDQ), a baseline EKG is recommended. If such patients have a known QT prolongation, hypokalemia (low potassium), or are being considered for other drugs that prolong the QT interval (e.g., moxifloxacin [MXF] and/or clofazimine [CFZ]), a cardiology consultation should also be obtained.
- **Psychosocial assessment:** Assess for existing mental health and social conditions that may impact treatment. See section: **Psychosocial Support**.



## Initial patient education

Many people will only be able to process a small amount of information during the diagnosis and early treatment period. Constant education and support will help patients and families to anticipate toxicities and to tolerate inconveniences during the long course of treatment.

**The first phase** of treatment is likely to be quite intensive as the patient may be very ill, in airborne infection isolation, and facing many toxic drugs. If the patient's primary language is not English, identify and secure a trained interpreter to assist with the delivery of this initial patient education:

- **Assess patient's understanding** of the diagnosis and plan for treatment
- **Involve the family** and/or significant others in provision of initial patient education
- **Keep information simple** with a focus on the following: gaining mutual commitment to the case management plan; minimizing transmission; obtaining information about contacts; and explaining legal requirements

### Help the patient to understand:

- He/she may feel worse before they feel better.
- The toxicity **symptoms will diminish over time** as the patient's body adjusts to the treatment.
- **Steps can be taken to minimize the side-effects** if and when they occur.
- In the long run, the **treatment will cure the disease**, save the patient's life, and prevent transmission to loved ones.

## Use of case management tools

### ***Drug-O-Gram, MDR-TB Monitoring Checklist and Case Management Plan***

The case manager should develop an individualized case management plan based on the patient's treatment regimen, co-morbidities, and psychosocial assessment. The plan format may vary among health departments depending on their record-keeping processes. Specialized tools such as the ***Drug-O-Gram*** and the ***MDR-TB Monitoring Checklist*** can be part of the case management plan to organize data regarding prior treatment, evaluation, and other notable events in a concise, summarized fashion.

The ***Drug-O-Gram*** is an important case management tool for following the patient's progress through TB treatment. The ***Drug-O-Gram***:

- Documents previous and current drug treatment, weights, microbiology including molecular results, radiology and DST results, and other important information in an easy-to-read, summary format.
- See **Tool 1: *Drug-O-Gram***.

Drug-resistant TB, particularly MDR-TB, requires that close attention be paid to the patient's response to treatment as well as prompt remediation of adverse events that may

arise. A monitoring checklist can help the case manager keep track of the various required examinations as the patient moves through treatment. The individualized **MDR-TB Monitoring Checklist**:

- Delineates the important monitoring events that should occur throughout treatment to assess for clinical response to treatment as well as toxicity based on the patient's drug regimen and underlying comorbidities.
- Ensures that elements of care are not neglected and can be reviewed with patients so they can anticipate upcoming events.
- See **Tool 2: MDR-TB Monitoring Checklist**, for a sample of how this checklist can be customized for individual patients.

**Use a systematic approach to monitoring.**

## Monitoring throughout treatment

Patients with drug-resistant TB will require regular monitoring throughout treatment to document sputum culture conversion and to watch for the development of toxicities. Patients should also be monitored closely for signs of treatment failure. The case manager is responsible for ensuring that all necessary monitoring for both toxicity and clinical response occurs and that abnormal results are brought to the attention of the treating clinician. See **Chapter 9, Adverse Reactions**.

## Monitoring treatment response

Monitoring response to treatment is done through regular evaluation of microbiology results, symptoms, weight, and radiography and other imaging.

TABLE 1.

## Activities for monitoring treatment response for MDR-TB

Adapted from: *Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis*, 2014

Monitoring evaluation	Recommended frequency
<b>Evaluation by clinician</b>	<p><b>During the intensive phase:</b> Every day during the first weeks if hospitalized and at least every week if treated as outpatient, until the treatment is well tolerated.</p> <p>Once stable, the patient is seen twice a month or once a month.</p> <p><b>During the continuation phase:</b> Monthly assessments unless there is a medical necessity to see the patient more often. The DOT provider sees the patient daily between consultations and signals any concerns to the case manager and clinician.</p>
<b>Treatment adherence and tolerance</b>	Daily at every DOT encounter by the DOT worker.
<b>Sputum smears and culture</b>	Obtain 3 sputa at the start of treatment and every 2 weeks until smear conversion, followed by 2-3 sputa every month until culture conversion, and then at least 1 sputum monthly throughout treatment.
<b>Weight</b>	At start of treatment, weekly until stable, and then monthly throughout treatment.
<b>Height</b>	At start of treatment for all (to be able to assess lean body weight or BMI); monthly for children (to assess growth).
<b>Drug-susceptibility testing (DST)</b>	At baseline for first- and second-line anti-TB drugs. Repeat DST for patients who remain culture-positive at month 3 or revert after month 4 (see <b>Chapter 2, <i>Diagnosis</i></b> for more information on DST).
<b>Chest radiograph</b>	At baseline, every 3 to 6 months during treatment, and at the end of treatment.

### Microbiology

Monitoring microbiologic response to TB treatment is essential in adult patients with pulmonary disease. Even for drug-susceptible disease, the prompt conversion to culture-negative sputum is very reassuring and allows for the use of short-course TB therapy. For drug-resistant disease, monitoring of sputum for smear and culture positivity is even more important.

- Most MDR-TB patients who are adherent to an effective regimen will convert cultures to negative within 3 months. Patients with fewer effective drugs in their treatment regimens (e.g., XDR-TB patients) will convert more slowly.
- At the start of treatment, obtain 3 sputa for AFB smear and culture. Sputum specimens should be collected at least 8 hours apart. At least 1 specimen should be an early morning specimen. Some patients will be able to produce higher quality specimens if all of them are collected first thing in the morning. Consider supervision of collections and/or sputum induction.



- Repeat sputum collection every 2 weeks until smear conversion.
- Once AFB smears become negative, continue to collect 2 to 3 sputum samples monthly until TB cultures become negative.
- Once the culture has consistently converted to negative, obtain **at least 1** specimen of sputum for AFB smear and culture **monthly** throughout the remaining course of treatment, and more frequently if indicated. Keep track of these smear and culture results using tools such as **Tool 1: Drug-O-Gram** and **Tool 3: Bacteriology Flow Sheet**.
- Whenever sputum is being collected, give appropriate attention to infection control. Collect sputum in a secure isolation area or an outdoor environment. **If the patient cannot spontaneously expectorate sputum, perform sputum induction with hypertonic saline in an appropriately engineered environment.**
- Serial culture collection in children can be difficult. For information on the best methods for collecting specimens for smear and culture in children, see **Chapter 6, Pediatrics**.
- Obtain sputum for AFB smear and culture at the end of treatment.
- An important activity of the case manager is coordination of microbiologic evaluation for the patient's cultures. Specimens should be of good quality and at least 5 to 10 mL in volume. Route specimens to the appropriate reference laboratories, request tests for specific detection of drug resistance, and communicate results as quickly as possible to the treating clinician.
- Patients whose sputa are still culture-positive after 3 months of treatment should be reevaluated fully, including repeat DST for the possibility of further development of resistance. Patients are considered to have failed therapy when their sputum cultures are still positive after 4 months of treatment. See section: **Assessment for treatment failure**.

## Extrapulmonary TB

Microbiologic monitoring of **extrapulmonary** disease is more difficult, and serial biopsies or aspirates are rarely indicated. However, if the patient is not responding to treatment, or if there is any reason to suspect that the treatment is failing, strongly consider repeat specimen collection.

## Symptoms

*“The classic symptoms of TB—cough, sputum production, fever and weight loss—generally improve within the first few weeks of treatment.”*

—WHO Companion Handbook

- Early in the course of treatment, assess for symptoms of TB weekly, and then monthly throughout treatment thereafter.
- Document resolution of symptoms that were present at diagnosis.
- Patients with chronic, progressive symptoms such as cough, fever, chest pain, and weight loss will often notice improvement or resolution of these symptoms within weeks of starting effective treatment.

### Systemic symptoms

- Assess and monitor improvement of the following symptoms commonly reported in TB patients: **fever, loss of appetite, pain, and fatigue.**
- Monitor TB site-specific symptoms, and document changes from baseline findings; for example, headache, vomiting, and neurologic changes are seen with central nervous system (CNS) disease.
- Screen for symptoms of co-morbid conditions, especially diabetes and HIV.
  - While initial immune reconstitution may exacerbate TB disease, the long-term health of the patient and ability to **cure** TB disease relies on the successful treatment of HIV.
  - HIV, diabetes mellitus, and other diarrheal and malabsorption syndromes affect drug absorption and may undermine TB treatment, resulting in treatment failure, amplification of drug resistance, or increased risk for relapse. If a patient is at risk for poor absorption, monitor for diarrhea and other symptom changes. For more information, see **Chapter 7, Co-morbidities and Special Situations.**

### Respiratory symptoms

Routinely monitor the patient's cough, respiratory status, and sputum production. Most MDR-TB patients' respiratory symptoms should begin to improve within weeks of starting on appropriate MDR-TB treatment.

**Investigate failure to improve or return of respiratory symptoms after initial improvement. Consider all the following possibilities:**

- **Other respiratory infection or process** (e.g., malignancy)
- **Non-adherent with therapy or not achieving therapeutic concentrations**
- **TB treatment failure? If failure is suspected:**
  - Repeat cultures and DST, including rapid molecular diagnostics for additional acquired resistance
  - Consider a regimen change (**never add a single drug to a failing regimen**)
- **Interpret respiratory symptoms in the context of the entire clinical picture:** fever curve, weight gain, other systemic symptoms, co-morbidities, and microbiologic response to treatment

### Weight

Many patients with TB are poorly nourished. This is especially pronounced in patients who have developed drug-resistant disease over years of failed treatments or have had long delays in diagnosis. Weight and nutritional status are important markers for disease status; addressing them is an important aspect of therapy.

- Check weight weekly until weight gain stabilizes, and then monthly throughout the course of treatment and follow-up.
- Lean body weight may be calculated for obese individuals to adjust medication dosage. BMI may be calculated for underweight patients to assess nutritional status.

- Occasionally, patients will lose weight while on treatment due to side effects; monitor patients closely to ensure no other signs of treatment failure and investigate the likely cause.
- Very young children with drug-resistant TB may need more frequent weight monitoring as well as monitoring of other indices of growth and development.

**NOTE:** Drug dosages may need to be adjusted as weight changes, particularly in young children and patients who have sustained significant weight loss prior to diagnosis.

### Nutritional support and use of supplements

- Maximize the nutrition of undernourished patients.
  - Offer hospitalized patients flexible meals of their choice, solicit dietary consultation, and offer dietary supplementation.
  - Some patients feel best and gain the most nutritional benefit from small, frequent meals (mini-meals) throughout the day.
  - Occasionally, tube feedings for supplementation are required, and rarely, parenteral nutrition is used (especially prior to surgery to improve post-operative healing).
- Customize outpatient management based on the nutritional status of the patient. Some patients will only need to have their weights monitored, and others will require food diaries, regular nutritional labs, and ongoing nutrition consultation.
- Consider cultural differences and arrange for foods to which the patient is accustomed.
- Some food supplements (such as Ensure and multi-vitamins) interfere with absorption of fluoroquinolones and should be offered at least 2 hours before or after the drug.
- Refer patients with co-morbidities affected by nutritional intake (such as diabetes) for dietary consultation.

### Radiography

Radiographic response to TB treatment lags behind clinical and microbiologic response.

#### Obtain routine chest radiographs:

- Every 3 to 6 months during treatment
- At the end of therapy
- 6, 12, and 24 months after treatment is completed or as clinically indicated

Additional radiographs are sometimes obtained when the patient has a clinical decompensation or co-morbidities. CT scans and special views (lordotic or bilateral obliques) may be useful for individual cases.

**In particular, CT scans should be obtained to assist in evaluating the differential diagnosis or when a more accurate assessment of the extent of disease is needed for surgery, duration of treatment, or unexplained changes on the chest radiograph.**

CT scans may be particularly useful for following lymph node and mediastinal disease, as well as extensive pleural and parenchymal changes. In very complex cases, an end-of-treatment CT is often useful as a baseline for future follow-up. Radiographs (plain films, CT, or MRI) are particularly useful in monitoring response to treatment for patients whose disease cannot be followed microbiologically:

- **Intracranial lesions**
- **Abscesses**
- **Bone disease**
- **Pleural disease**
- **Deep lymph nodes**

## Assessment for treatment failure

Patients are considered to have failed therapy when their sputum cultures are still positive after 4 months of treatment.

### **When AFB smear or culture positivity persists or recurs, address and consider:**

- Adherence to therapy
- Accurate dose calculation and administration
- Drug absorption
- Adequacy of the drug regimen
- Development of acquired resistance
- Respiratory and constitutional symptoms
- Radiographic findings
- Possible poor penetration of drugs into a localized area (e.g., empyema, thick-walled cavity in poorly vascularized lung)
- Presence of conditions that may delay culture conversion (e.g., uncontrolled diabetes, malabsorption, extensive disease)

## Monitoring for drug toxicity

Screening for drug toxicity and adverse effects is an important part of MDR-TB treatment. Close monitoring is needed to ensure side effects are responded to promptly, particularly when treatment is initiated in an outpatient setting.

### General principles

- **Counsel every patient** beginning any TB therapy to anticipate toxicity.
  - Even patients taking INH monotherapy frequently feel poorly in the first few weeks of therapy. If patients do not anticipate this reaction and are not reassured that it will improve, they may stop the therapy.
  - Monitor patients for general toxicities and drug-specific toxicity at every health-care visit (including during DOT encounters). See **Tool 2: MDR-TB Monitoring Checklist**.
  - Patients with drug-resistant TB may experience more toxicity than patients treated for drug-susceptible disease. Most of the second-line TB drugs are associated with significant side effects.
- Take measures to minimize toxicity and to help patients tolerate the toxicity rather than losing the drug in the regimen. In many cases, there are no alternative drugs for replacement.
  - **Supplemental ancillary medication** can be helpful in addressing some common side effects.
  - **Non-pharmaceutical approaches** should also be considered. Examples might include:
    - **Change the timing of the dose** to minimize toxicity (e.g., dose at bedtime).
    - **Dose some medicines with food** (have patient try different foods to find something palatable).
    - **Relaxation techniques** can sometimes be helpful.
  - See **Chapter 9, Adverse Reactions**, for approaches to address common adverse events.

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**NOTE:** While most drugs can be continued safely, in general, a patient who suffers **vestibular toxicity** from an **aminoglycoside** or **capreomycin (CM)** should not receive those drugs in the future.

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### Routine toxicity monitoring

Screening is necessary to detect adverse effects that are not apparent through physical exam or observed by the patient. For patients with MDR-TB or XDR-TB, routine monitoring for drug toxicity frequently includes the following:

- **Screening for bone marrow suppression:** Complete blood counts intermittently as clinically indicated; monthly for patients on **linezolid (LZD)**.
- **Monitoring renal function:** Creatinine at least monthly for patients receiving **aminoglycosides** or **CM**.
  - Baseline creatinine clearance should be documented in persons with serum cre-

atinine greater than expected, or if any concerns arise. (See **Chapter 5, Co-morbidities and Special Situations, Renal Failure, Table 1**, for creatinine clearance calculations.)

- Calculate creatinine clearance especially for patients with small body weight, older age, and in those with diabetes.
- **Monitoring liver function:** Liver function tests (LFTs) monthly (AST, ALT, total bilirubin) for patients taking **pyrazinamide (PZA)**, **ethionamide (ETA)**, or **para-aminosalicylate (PAS)**.
- **Monitoring serum electrolytes:** Potassium, calcium, and magnesium monthly for patients on **CM** and **aminoglycosides**.
- **Screening for hypothyroidism:** Thyroid function (TSH) every 3 months for patients receiving **ETA** or **PAS**.
  - Monitor TSH sooner if symptoms of hypothyroidism develop or if baseline thyroid testing shows abnormalities.
  - Use thyroid replacement if hypothyroidism is documented.
- **Screening for hearing loss and vestibulopathy.** Assess audiometry and vestibular function monthly for patients receiving **aminoglycosides** or **CM**. See **Tool 6: Hearing and Vestibular Screening Flow Sheet** for a sample tool that can be used to assess vestibular function and keep track of monthly vestibular and audiogram screening results. A change in hearing or vestibular function from baseline should be brought promptly to the treating clinician's attention, and the patient should be referred for further evaluation. Some sequela resulting from ototoxicity can be permanent (hearing loss, vertigo, and tinnitus). Early identification and referral is important to enable appropriate modification to the drug regimen to limit or prevent these outcomes. See **Chapter 9, Adverse Reactions**, for information on the management of ototoxicity.
- **Screening for visual changes:** Screen monthly for visual acuity and color discrimination for patients on **ethambutol (EMB)**, **LZD**, and **CFZ**. Refer a patient for further evaluation if changes in vision (acuity or color) or complaint of eye pain is noted. See **Tool 5: Vision Screening Flow Sheet** for tracking of monthly visual acuity and color vision screening results. Watch for evidence of uveitis for patients on **rifabutin (RFB)**.
- **EKG** at least 2, 12 and 24 weeks into treatment for patients on **BDQ**, or weekly if **BDQ** is combined with other medications that may prolong the QT interval.
- **Screening for peripheral neuropathy:** Monitor for peripheral neuropathy monthly while patient is on **LZD** and as clinically indicated for patients on fluoroquinolones (or high-dose INH).
- **Screening for depression, agitation, and psychosis:** Monitor for depression and mood changes (including agitation) monthly for patients taking **cycloserine (CS)**. The most common toxicities associated with CS are depression, psychosis, and suicidal thoughts. Standardized tools for assessing and documenting mental health symptoms are very helpful. It is also important to educate family members to notify the case manager or clinician if they notice any changes in the patient's mood since the patient may not be aware of these adverse effects. See **Resources** at the end of this chapter for examples of screening tools.

See **Tool 2: MDR-TB Monitoring Checklist** and **Chapter 5, Medication Fact Sheets**.



## Drug interactions

Many drugs interfere with TB therapy or contribute to toxicity.

- Monitor patients as to any new medication started. This should include over-the-counter therapies such as:
  - Vitamin/mineral supplements
  - Antacids
  - Traditional medicine, home remedies, and “alternative” or herbal supplements

## Therapeutic drug monitoring

The case manager also frequently coordinates collection and transport of blood samples for therapeutic drug monitoring. Few reference laboratories perform these levels, and factors such as cost and a patient’s insurance status require the expertise of the case manager. For details about timing of blood draws, processing, and shipping of samples, see **Chapter 3, Laboratory**, section on **Therapeutic Drug Monitoring**.

Situations in which serum drug concentrations are commonly used:

- In patients with known **renal insufficiency**
  - **Aminoglycoside** concentrations—target trough drug concentrations are generally <5 mcg/mL in patients. (With the once-daily dosing used for treatment of TB, this is seldom an issue for patients with reasonably normal renal function. Some experts routinely monitor aminoglycoside peak concentrations in all patients.)
  - **EMB** concentrations (when it may be necessary to use this drug in patients with significant renal impairment).
- When using **second-line drugs with a narrow therapeutic window** in order to achieve target concentration and minimize toxicity
  - **CS** concentrations, particularly early in the course of treatment, can help the clinician to determine appropriate dose, minimize CNS adverse reactions, and prevent seizure activity. Target concentrations are ideally between 20–30 mcg/mL (below 35 mcg/mL to help avoid CNS side effects). Dose initiation may be done in a “ramped” manner; see **Chapter 4, Treatment**, section on **Escalation of Dosages (Drug Ramping)**.
  - Some experts may also routinely check **ethinionamide** and **PAS** levels.
- When few effective drugs are available to include in the regimen, in order to optimize the effect of available drugs
- In patients with co-morbid conditions in which there may be known or suspected malabsorption or when a patient fails to show clinical response to treatment (i.e., remains culture-positive despite appropriate drug regimen, doses and DOT)
- When there is concern for potentially significant drug-drug interactions (such as rifamycins and antiretrovirals)

## Monitoring tools and strategies

As previously noted, the use of monitoring tools will help keep track of the many details of case management, enabling the case manager and treating clinician to keep results organized, to anticipate problems and manage them as they occur. Additional helpful strategies include:

- **Scheduling regular visits** with the patient, initially weekly and then monthly, to perform a thorough assessment until treatment is completed.
- **Real-time reminders** on the computer or mobile phone, a tickler system, etc.
- Seeking **expert consultation** from regional resources such as state TB Control programs and Regional Training and Medical Consultation Centers (RTMCCs). The learning curve is very steep during case management of the first case or two of drug-resistant TB, and use of the resources included in this book and discussions with experts will help with the rapid acquisition of information required. See **Appendix 1: Expert Resources for Drug-Resistant TB**.

## Post-treatment monitoring

At the end of treatment, a sputum culture and chest radiograph (CXR) should be obtained. The patient should undergo post-treatment monitoring for a minimum of 2 years to monitor for relapse. At 6, 12 and 24 months post-treatment (or as clinically indicated), the patient should be monitored with:

- Symptom review
- Medical evaluation
- Sputum for AFB smear and culture
- Chest radiograph

## Patient-centered care and ensuring adherence

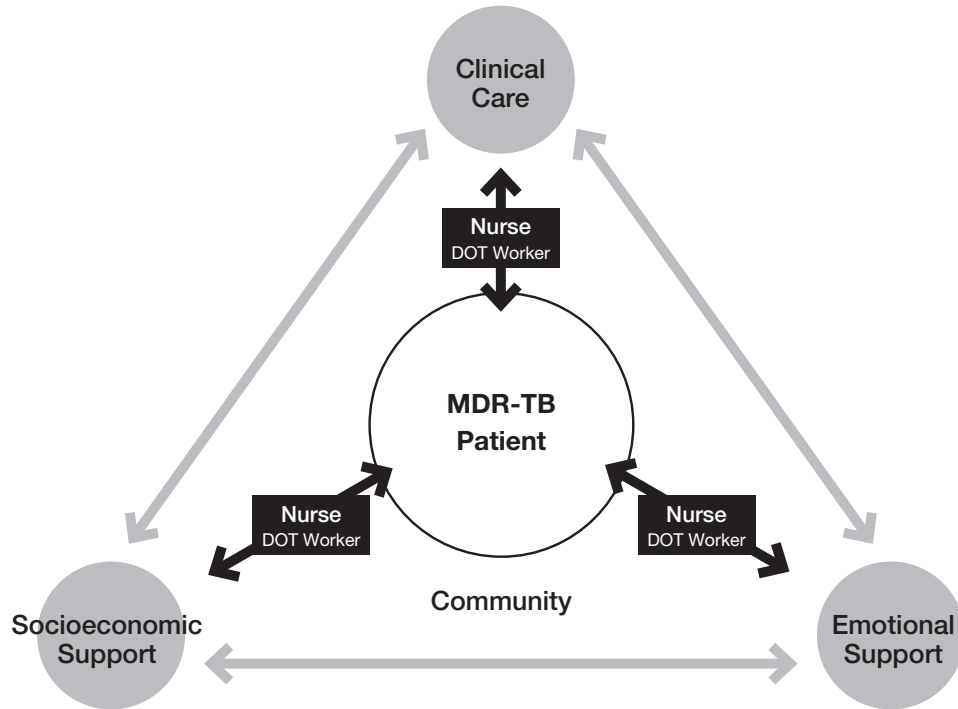
### Standard 9 of the *International Standards for TB Care*

*“Patient-centered approach to treatment should be developed for all patients in order to promote adherence, improve quality of life, and relieve suffering. This approach should be based on the patient’s needs and mutual respect between the patient and the provider.”*

Model programs utilizing a case management and patient-centered care approach in community-based care of drug-resistant TB patients (Figure 1) demonstrate high levels of treatment success.

FIGURE 1.

## Community-Based Model of MDR-TB Treatment



Adapted with permission from *The Community Based Model of Multidrug-Resistant Tuberculosis Treatment*, Jaime Bayona, MD, MPH, Socios En Salud Sucursal, Peru

Adherence to MDR-TB treatment is essential to prevent the amplification of resistance, to increase the chances of treatment cure, and to prevent ongoing transmission in the community. Even in high-resource settings, adherence to MDR-TB treatment can be challenging due to the long duration of treatment, the frequent and serious side effects, and the social and economic burdens to patients and their families.

A variety of factors influence adherence to treatment, including: the provision of DOT; the individual's knowledge and beliefs; social and emotional support available to the patient; and economic support to cover the cost of treatment and potential loss of income to the patient and family while the patient is unable to work or attend school. In order to promote adherence and support the patient, the case manager will be providing or coordinating the following activities:

- **DOT** (including arrangements for the injectable agent)
- **Information support** (education to the patient and family)
- **Psychological/social support** (including use of culturally appropriate resources)
- **Material support** (including use of incentives and enablers, and linkage to health care coverage)
- **Use of legal orders** when indicated

## Directly observed therapy (DOT)

The consequences of treatment failure and further acquired drug resistance make DOT **a high priority for cases of drug-resistant TB**. DOT is the most effective strategy for ensuring patients take their medications correctly. It is recommended as a standard of care worldwide. Achieving this standard of care, however, requires far greater time and commitment in the setting of drug-resistant TB than of drug-susceptible disease. Weekend doses, drugs given more than once a day, and drugs tolerated only at bedtime will provide programmatic challenges, and DOT may need to be a shared responsibility.

*DOT is so important to the treatment of drug-resistant TB that experts in the field of TB control around the world consider it an essential strategy.*

DOT means that a health care worker or other designated individual watches the patient swallow every dose of the prescribed regimen. Since there are often many pills to swallow, DOT workers will need ample time to sit with the patient. The DOT worker may also be observing that the patient completes the infusion of the injectable agent when patients have been taught to administer the infusion at home. See section: **Roles and responsibilities—DOT worker**.

The case manager must keep an open line of communication with the DOT worker and ensure that he/she can assess which signs and symptoms indicate potential medication toxicity.

- When the case manager is not the individual actually providing the DOT, **regular contact with the DOT provider and weekly contact with the patient will be important during the initial phase** to ensure that the patient is tolerating the medication and that side effects are quickly addressed.
- While most patients will experience mild complaints that can be managed without a change in the drug regimen (e.g., initiating adjuvant therapy, changing dosing time), some side effects warrant at least temporary discontinuation of the offending drug. Any toxicity must be quickly identified, reported, and acted upon (see **Chapter 9, Adverse Reactions**). Address all complaints, even if no change can be made.
- It is very important to use standardized forms to record DOT doses and toxicities for these complicated patients.
- Some programs have patients complete a DOT acknowledgement or patient contract so that expectations are clearly explained and agreed upon.

*No detail regarding medication administration should be assumed or left to chance.*

### Routinely ask patients:

**“How did you take your medication?”** (when medications are taken over the weekend or when the dose is self-administered)

**“Have you eaten any milk-based products, antacids, or vitamin products within 2 hours of taking medications?”** (these inhibit the absorption of fluoroquinolones)

**“Did you throw up after taking your medicine?”** (important to ask even if medications are given by DOT in case the patient is vomiting after the DOT worker leaves)

## Providing the injectable agent

Arranging for and providing the administration of an injectable agent for MDR-TB patients can be challenging as many local health departments are not staffed to provide either infusions or injections. Although providing the injectable agent may be daunting, it is important that the patient and staff understand the importance of the injectable agent in the regimen.

### INJECTABLE AGENTS

**Why:** Bactericidal agent

**When:** 5-7 times per week at start of treatment, often drops to 3 times per week after culture conversion to minimize toxicity

**Where:** Hospital, home, clinic, infusion center

**How:** Intramuscular (IM) or intravenous (IV)

**How long:** Usually 6 months post culture conversion unless toxicity develops

A number of factors contribute to the decision for whether the patient will receive the injectable agent as an IM injection or via a peripherally inserted central catheter (PICC), including: insurance, patient preference, health department capacity to provide injection or infusion, DOT arrangements, and availability of home health for IV infusions. Patients without health insurance are often unable to afford placement of a PICC line, and IM injections may be the only option. If there is the choice of either IM or IV administration, patient preference should be strongly considered in addition to safety concerns, ability to provide DOT of the injectable agent, and logistics.

### IM injections

Initially, staff may be skeptical that a patient can tolerate IM injections for 6-plus months. However, many MDR-TB programs in the United States and internationally administer IM injections for all their MDR-TB patients with excellent outcomes. Some programs provide the IM injection in the patient's home, which can be more comfortable and convenient for the patient. Alternatively, patients can come into the clinic/provider office to receive the injection as long as appropriate infection control is in place while the patient is still infectious. Public health and/or clinic nursing staff may require additional in-service training if they have not had recent experience in providing injections. Good injection technique can make the experience less painful for the patient. Lidocaine can be added to the injection to lessen the pain. See **Resources** at the end of this chapter for additional information.

### IV infusions

Patients may prefer to receive infusions versus IM injections. A major challenge in providing infusions is finding staff to perform the infusion. Typically, public health nurses are not trained to provide infusions—or it falls outside of their scopes of practice—and a home health agency may be needed to provide home-based infusions. Often, home health agencies train family members to administer medications; the agencies visit once-a-week to assess the insertion site of the PICC line (or other intravenous catheter) and provide the supply of medications. It is important that the case manager communicate closely with

the home health agency regarding the assessment of whether the patient or family member can safely administer the infusion using proper clean technique.

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**NOTE: Amikacin (AK) may be a better option than capreomycin (CM) for home infusion.** Pharmacies typically provide premixed solutions of AK as it remains stable at room temperature for at least 3 weeks. Patients receiving CM may need to learn to reconstitute the powder as it is not considered stable after 24 hours upon refrigeration (refer to package insert for full instructions).

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Even if the case manager is not directly administering the infusion, it is important that he/she be aware of and assess for signs of infection. Additionally, when the patient or family member administers the infusion, arrangements for DOT of both parenteral and oral medications are needed. Some programs coordinate the DOT of the oral medications with the timing of the infusion. For example, the DOT worker arrives as the infusion is finishing. Programs should establish protocols and procedures for the DOT workers to document administration of the infusion. Once a patient is no longer considered infectious, another option is to use an infusion center.

### Calculating the concentration and volume for administering injectable agents requires careful attention.

For example: CM comes in a powder form and when the diluent is added, the volume expands (i.e., exceeds the volume of diluent added).

**CASE EXAMPLE:** Patient who weighs 55 kg has an order to receive 15 mg/kg CM (825 mg) IM 5 days per week. The nurse reviews the packet insert and sees that when 3.3mL diluent is added to the 1g, 10mL vial, the concentration is approximately 260 mg/mL.

The nurse performs the following calculation to determine the volume of solution to inject to provide 825 mg of CM:

$$260 \text{ mg} / 1 \text{ mL} = 825 \text{ mg} / x \text{ mL}$$

$$X \text{ mL} = 825 \text{ mg} / 260 \text{ mg}$$

$$X \text{ mL} = 3.17 \text{ or } \mathbf{3.2 \text{ mL solution}}$$

It is important for the nurse to review the package insert for each injectable medication to determine the appropriate volume.



## Patient education

All patients and their family members should receive education about MDR-TB, its treatment, and the need for adherence to therapy. Education may be provided by physicians, nurses, community health workers, and other health care providers. The case manager will have a key role in providing education, coaching, and support to the patient throughout treatment. Health care providers are encouraged to communicate with patients in a manner that is respectful, supportive and helps to build a positive partnership. Providers should avoid “talking at” patients and refrain from language that is judgmental or punitive (e.g., “If you don’t take your medications, you will make other people sick...”).

*Ongoing TB education is essential...*

### Tips for delivering key information to the MDR-TB patient

- Always use a venue that guarantees confidentiality in communication.
- Use language that promotes mutual respect and esteem between the patient, caregivers, and health-care providers.
- Do not make promises that the health-care service cannot keep.
- Respect the patient’s right to choose.
- Enable the patient to counteract stigma and discrimination by reassuring that his/her disease is not the result of any socially or morally inappropriate behavior that he/she has made in the past, and that many other patients have successfully completed treatment.

Adapted from: *Companion Handbook to the WHO Guidelines for the Programmatic Management of Drug-Resistant Tuberculosis*, 2014

The following phases may not fit the treatment course for all MDR-TB cases, but will provide a context for case managers to anticipate their patients’ educational capacities and needs. The analogy of preparing for a marathon has been suggested to emphasize the key role the case manager can play in coaching the patient through the various phases of treatment and by setting achievable interim goals.

### 1. First phase

The first phase spans from diagnosis through the period of time the patient may require airborne infection isolation. (See section: **Initiating treatment, initial patient education**). If the patient’s medical needs are not given careful attention during this first phase, the patient is at higher risk for becoming discouraged. Information to share and discuss includes:

- **Major concepts:** MDR-TB, like regular TB, is a contagious disease, which means it can be spread from person to person. TB generally lives in the lungs, but it can also infect other parts of the body. If MDR-TB is left untreated, it can kill the patient. **MDR-TB can be cured** with the right medicine.
- **Recognize and address the patient’s fears and concerns.** Patients are less likely to comprehend treatment information if they are fearful or preoccupied with worries about their jobs or family members.

- **Clarify how drug-resistant TB can be transmitted and how it cannot be transmitted** (i.e., not through sexual relations, sharing food, etc.).
- **Simple infection control practices**, such as covering the mouth when coughing.
- **Airborne infection isolation plans, strategies for keeping the home well-ventilated** with fresh air, and adhering to visitor restrictions if isolated at home.
- Patient's **plans regarding work, travel, or moving**.
- **Expected side effects** and what to do should they occur, including reporting to the DOT provider.
- **How to contact the DOT worker, case manager and/or clinician** in case of an urgent issue when the health department is closed.
- **Available educational and social support resources** in the community and online as appropriate. See **Resources** at the end of this chapter.
- **Criteria for non-infectiousness** (i.e., when home isolation can be discontinued per program protocols and the patient will be allowed to return to work or school).

## 2. Second phase

Once the patient is stabilized on treatment, the emphasis of education will shift. During this phase, **focus on helping the patient manage any side effects, maximizing nutrition** and working together to **identify barriers to adherence**. Drug toxicity can occur at any phase in treatment and should continue to be closely monitored. If surgical intervention is indicated, it might occur during this phase. Information to share and discuss includes:

- **Patient's knowledge and understanding of the disease, treatment plan** and potential serious side effects of treatment
- **Management of side effects** (see **Chapter 9, Adverse Reactions**)
- **Arrangements for DOT and clinical response monitoring**
- **Incentives and enablers** that might aid adherence to treatment (see section: **Use of incentives and enablers**)
- **Management and care for co-morbid conditions**
- **Appetite, nutritional status, and physical activity** as tolerated
- **Signs of clinical improvement**
- **Management of injection site(s)** (care of IM/IV sites)
- Patient's **plans concerning work, travel, or moving**

## 3. Third phase

If continued clinical response is achieved, the third phase begins when the parenteral agent is discontinued and lasts until the end of treatment. While this may sound much like nearing the home stretch, it is really closer to passing the halfway point. The patient may have another year or more of oral medication to complete before reaching the finish line. Information to share and discuss includes:

- Patient's plans concerning work, travel, or moving
- Management of side effects (different side effects may develop later into therapy requiring additional management and sometimes a change of medication)

- **Arrangements for DOT and clinical response monitoring**
  - As the patient's circumstances change (e.g., return to work), make necessary adjustments in collaboration with the patient
  - Continually reassess the patient's belief in and understanding of the importance of uninterrupted treatment to prevent treatment failure and relapse
- **Identifying acceptable interventions and strategies for addressing potential barriers** as needed

#### 4. Final phase

The final phase begins once treatment is completed. The marathon is over, yet the patient will require clinical monitoring for the next 2 years to ensure that if a relapse occurs, it will be identified and acted upon quickly. Information to share and discuss includes:

- Ensure that the patient is **knowledgeable about signs and symptoms of TB and what to do** should he/she experience them.
- **Schedule and inform the patient of follow-up appointments.** Arrange for reminder notification suitable to the patient.
- Revisit the patient's **plans concerning work, travel, or moving.** Provide the patient with appropriate referral and contact information as indicated.

### Psychosocial support

Patients with MDR-TB face many stressors, including the diagnosis of a potentially life-threatening disease, issues of stigma, serious side effects, and economic hardships. A 2006 report by Chalco and colleagues found that many patients with MDR-TB experience strong feelings of guilt and in some cases, the stigma may not come from the social surrounding, but rather from the patient's own family; relatives may react in accordance with past experiences and cultural beliefs. Most patients will need ongoing social and emotional support to cope with these challenges. The case manager often plays a key role in providing emotional and social support by listening to the patient, and talking with patient and family to reduce stigma, fear, and misunderstandings about the disease.

Engage family members in the patient's care; encourage and praise their support. Do everything possible to get the family to cooperate and support the treatment plan. An investment of time initially is well worth the benefits it often reaps. Offer to evaluate family members for TB or latent tuberculosis infection (LTBI) and answer their questions.

Assess the patient's social support network and the strengths and barriers to adherence. Ensure that plans are in place for addressing issues such as mental illness, substance abuse, and homelessness.

Consider community services that can assist you in addressing these challenges:

- Social services and programs for the medically indigent
- Community-based organizations
- Immigration law counsel
- Drug and alcohol counseling
- Mental health programs

Your key to successfully assisting patients with these challenges is to develop a trusting relationship with the patient and to be familiar with resources in your community. Ideally, case managers will have familiarity with and ongoing relations with valuable community resources prior to their first cases of drug-resistant TB.

## Substance abuse and mental illness

Some TB patients are at higher risk of substance abuse and mental health issues. Substance abuse treatment programs are important partners with TB clinics and providers. Similarly, treatment of mental health disease is paramount in keeping patients adherent to TB therapy.

- Closely monitor a patient's success and/or relapse with substance abuse issues during TB treatment in order to anticipate toxicity and to avoid adherence complications. Facilitate referral to programs and services that can work with the patient on harm reduction.

Even patients without underlying mental health issues will need significant mental health support and monitoring during the long and arduous treatment for drug-resistant TB. Situational depression can affect many patients and can be quite debilitating. **CS**, which is often used to treat MDR-TB, is known to be associated with significant neurotoxicity resulting in depression and sometimes psychosis, particularly when serum drug concentrations are high. Monitor patients for these symptoms and provide support and referral as needed. See **Resources** at the end of this chapter for tools to monitor for depression and psychosis.

- Be aware that some drugs to treat depression such as **selective serotonin reuptake inhibitors (SSRIs)** are not recommended for patients on **LZD**.

## Cultural and religious background

The proportion of patients with MDR-TB in the United States who are foreign-born is substantial (approximately 90% in 2013). A patient's cultural background, spiritual traditions, prior experiences of treating illness, and history of access to care may impact how he/she views the path towards health. Assessing patients' understanding of and beliefs about their diagnoses and treatment plans can provide case managers and providers with important information to negotiate mutually acceptable approaches to treatment.

TABLE 2.

## Leveraging cultural- and religious-related resources during MDR-TB diagnosis and treatment

Examples of potential barriers	Strategies to build on cultural strengths
<ul style="list-style-type: none"> <li>• Cultural stigma about TB</li> <li>• Concern that the illness might interfere with immigration process and/or result in deportation</li> <li>• Hindered access to health care because of:               <ul style="list-style-type: none"> <li>• Lack of health insurance coverage and/or eligibility</li> <li>• Language or cultural barriers combined with the general difficulty of navigating complex health care systems in the United States</li> </ul> </li> <li>• Patient's preference to:               <ul style="list-style-type: none"> <li>• Seek traditional medicine and healing modalities when ill</li> <li>• Seek out a physician from his/her own culture, who may not be familiar with diagnosis and treatment of drug-resistant TB</li> </ul> </li> <li>• For women: Loss of importance to her family if she cannot continue her usual activities or if she experiences disapproval from her spouse</li> <li>• Fear of the diagnosis itself if the individual has lost a friend or family member due to drug-resistant TB</li> </ul>	<p><b>Explore local resources to help bridge the barriers and develop partnerships with the patient to facilitate communication and understanding:</b></p> <ul style="list-style-type: none"> <li>• Trained medical interpreters</li> <li>• Trained patient navigators</li> <li>• Bilingual health department staff</li> <li>• Cultural health brokers</li> <li>• Healthcare professionals from the patient's culture</li> <li>• Community leaders, community organizations</li> <li>• Church-based services</li> <li>• Traditional healers</li> <li>• Other local health departments with experience working with specific ethnic groups</li> <li>• Court interpreters, telephone-accessed interpreters, university language departments</li> <li>• Refugee health and social service programs</li> </ul> <p><b>Connect patients to supportive services and care:</b></p> <ul style="list-style-type: none"> <li>• Legal resources, especially immigration</li> <li>• Counseling services and/or peer support groups</li> <li>• Access to spiritual or religious counsel, particularly during the isolation period</li> </ul>

Few translated patient materials that pertain specifically to drug-resistant TB exist; however, there are a number of Internet sites offering general TB patient education material in various languages. Additional sites contain cultural information that may be helpful to the case manager in anticipating the patient's cultural practices and needs. See **Appendix 4, *Multicultural Resources***.

### Economic support

Patients with drug-resistant TB may face economic hardship due to the cost of treatment, loss of work, interruption in schooling, and stigma. Costs associated with the treatment and management of patients with drug-resistant TB may vary widely and are influenced by the amount and type of drug resistance as well as the extent of disease. For patients with limited or no health insurance coverage, charges associated with the cost of drugs, diagnostic exams, and surgery may pose an extreme financial burden on individuals and families.

## Health care coverage

- In states that have expanded Medicaid access under the Patient Protection and Affordable Care Act (PPACA or ACA), inpatient and outpatient TB care can be provided to adults who meet income and legal eligibility criteria through full-scope Medicaid. These patients also may be eligible for TB Medicaid that often provides outpatient services with no share of cost, in addition to full-scope Medicaid.
- In some jurisdictions, all TB care may be provided free of charge in the public health setting.
- Patients who are undocumented immigrants may also be able to enroll in full-scope Medi-Cal. See **Resources** at the end of this chapter for more information.
- Organizations that provide *pro bono* immigration legal services can be very helpful in exploring options available to undocumented persons or low-income immigrants.

Many patients experience a period of prolonged unemployment associated with the period of infectiousness and due to employment discrimination. The case manager may intervene and educate employers to help protect a patient's job during the period the patient must remain on respiratory isolation. The case manager may also be instrumental in assisting to find alternative sources of income and/or other assistance (i.e., obtaining disability benefits) for the patient and his/her family while he/she cannot work (see sections: **Patient assistance programs** and **Incentives and enablers**).

**Addressing any financial challenges early in the patient's course of treatment will go a long way in establishing a foundation of confidence and trust.**

## Patient assistance programs

The distribution of drugs used to treat drug-resistant TB varies throughout the country, with some states maintaining central purchasing and distribution. The cost of these drugs is also variable, but in general, they are expensive, particularly when you factor in the length of treatment. Patient assistance programs (PAPs) may be helpful in offsetting costs. Table 3 displays some drugs used to treat drug-resistant TB that are known to be included in PAPs. Please note that PAP information changes periodically and some offers are time-limited.

The AIDS Drugs Assistance Program (ADAP), funded by Ryan White CARE Act dollars, provides HIV-positive individuals with low- or no-cost prescription medications to treat HIV/AIDS and related conditions. In October 2007, ADAP announced that 8 drugs used to treat MDR/XDR-TB were added to the ADAP formulary: moxifloxacin, CM, ETA, CS, p-aminosalicylic acid, imipenem/cilastin, LZD, and levofloxacin. The ADAP formulary now includes most if not all of the drugs used to treat pan-susceptible TB and drug-resistant TB. To inquire about a patient's eligibility for this program, contact the local ADAP coordinator at the state health department.



TABLE 3.

**TB Medications and Patient Assistance Programs (PAPs)\***

Brand name	Generic name	Manufacturer / Assistance Program	Eligibility criteria	PAP telephone / contact information
Treactor-SC	Ethionamide	Pfizer/ RxPathways PAP	Resident of U.S., Puerto Rico, or Virgin Islands without insurance or under-insured	866-706-2400 www.pfizerrxpathways.com
Levaquin	Levofloxacin	Janssen Pharmaceuticals/ Johnson & Johnson Patient Assistance Foundation	Resident of U.S. or U.S. Territory without sufficient resources	800-652-6227 www.janssenprescriptionassistance.com/levaquin-cost-assistance
Avelox	Moxifloxacin	Merck Sharp and Dohme Corp.	U.S. resident without prescription insurance coverage <b>and</b> meets income stipulations	800-727-5400 Merck Helps PAPs www.merckhelps.com/Programs.aspx
Zyvox	Linezolid	Pfizer/Zyvox Assist	Resident of U.S. or Puerto Rico without insurance or under-insured	866-706-2400 Pfizer RxPathways www.pfizerrxpathways.com  My Pfizer Brands www.mypfizerbrands.com  Zyvox Assist: 855-239-9869 www.zyvoxassist.com Note: this is a one-time coupon that expires 12/31/2016
Augmentin	Amoxicillin/ clavulanate	GlaxoSmithKline/ Bridges to Access	U.S. resident, without resources	866-PATIENT 866-728-4368 www.bridgestoaccess.com
Lamprene	Clofazimine	Novartis	MDR-TB	301-796-8240 FDA, single patient Investigational New Drug (IND)

\*Please note: PAP information changes periodically. Information in this table is current as of October 1, 2015.

## Use of incentives and enablers

The use of **incentives and enablers** is another strategy reported to be effective in assisting patients in maintaining adherence to treatment. Enablers such as transportation and food vouchers can be used to address some of the economic hardships experienced during treatment. Additionally, patient motivation commonly wanes once the patient begins to feel better and may affect the patient's commitment to the treatment plan. Simple interventions geared at making the patient's experience easier, as well as that of their family, can go a long way towards gaining commitment to treatment.

For more information about incentives and enablers, see **Resources** section at the end of this chapter.

## Homelessness

When MDR-TB is diagnosed in someone who is homeless or at risk of becoming homeless, additional support is necessary to ensure stable housing can be procured and co-morbidities addressed and managed early on.

- A 2014 study by Marks, et al., indicated that TB patients who were recently homeless were 5 times more likely to acquire drug resistance during treatment than were patients without a recent history of homelessness.
- Closer monitoring of MDR-TB patients who have recently experienced homelessness may be necessary to ensure they are showing response to treatment.
- See **Resources** at the end of this chapter.

## Use of legal orders

Legal measures are sometimes required when a patient with infectious, drug-resistant TB remains non-adherent despite interventions to overcome barriers and to gain the patient's cooperation. The case manager should be knowledgeable about the process for referring such patients, and must ensure that all lesser restrictive measures that have been employed have been documented. When recalcitrance persists, local, regional, and/or state TB control programs can provide additional information on the state laws and regulations pertaining to TB.

# Continuity of care

The role of the case manager becomes increasingly important when the drug-resistant TB patient is being treated in the private sector and/or changes providers during treatment. When the drug-resistant TB patient moves between facilities (such as a hospital or jail) and the community during treatment, the case manager must ensure that appropriate treatment, monitoring, and education of the patient continues. This may require:

- Establishing relationships with a new group of staff
- Providing training and/or information on drug-resistant TB to staff caring for the patient
- Establishing processes for sharing information

## Hospitalization and discharge planning

Some patients may require inpatient admission to enable prompt management of drug side effects and adverse reactions.

- **If the patient is hospitalized, the case manager will need to provide support to the patient as well as to the hospital staff.** Hospital staff who do not care for TB patients routinely will need to be reminded to observe each dose of medicine (not to leave the medicine at the bedside) and may need to be educated about many aspects of drug-resistant TB care.
- Hospital staff should be encouraged to seek expert consultation when necessary.

Frequent and timely communication with the patient's hospital-based treatment team regarding **discharge planning** should include:

- Procurement of medications prior to discharge
- Plan for DOT
- Coordination of infusion therapy services if the health department cannot provide them
- Plan for home isolation if the patient will be discharged while still considered infectious (see **Table 4** and section on **Infection control—Home isolation** for further guidance when a patient is still considered infectious)
- Plan for addressing psychosocial issues (such as mental illness, homelessness and substance abuse)
- Scheduling of follow-up clinic appointments and monitoring tests, and providing a contact number to call should problems arise
- Ensuring the hospital is working with the patient to address **ongoing care of co-morbid conditions**, such as HIV, diabetes mellitus, and renal disease.

## Interjurisdictional transfers

If the patient moves out of the case manager's jurisdiction, concrete plans for transfer of care need to be in place before the move. Even if the patient moves out of country, an accepting provider and responsible jurisdiction need to be identified and apprised of the patient's disease and treatment history. (See **Resources** for CDC website on international notification of TB cases.) Provide the patient with enough medications to last through the travel period until he/she can re-establish DOT in the new jurisdiction. Contact information

for family and friends, both in your area and in the destination, may be helpful if the patient does not arrive at the destination in a timely manner.

As appropriate, consider referral to programs such as **CureTB** or **TBNet**. Both programs are available at no cost to patients or clinicians. These programs can work with patients who are considering a move prior to completion of therapy. **Note:** Availability of second-line medications, TB cultures, and DOT may be limited in some countries.

- **CureTB** is a binational referral program based in San Diego, California, for patients with TB who move between the United States and Mexico or Central America. CureTB will link patients to TB providers in the countries to which they are traveling, and will share relevant clinical information with the receiving providers.
- **TBNet** is an international tuberculosis patient navigation program under the Migrant Clinician's Network. This program is designed to provide bridge case management for mobile, underserved TB patients inside and outside of the United States. TBNet enrollment is strongly recommended for any MDR-TB patient with suspicion of movement. This program also provides a treatment outcome report to the enrolling site upon case closure. Note: TBNet requires patient consent for enrollment.

See **Resources** for contact information for CureTB and TBNet.

## Co-management with private providers

If the patient is managed by a private provider:

- Make an appointment to meet the provider and the office staff as soon as possible.
- Explain your role and legal responsibility to monitor the patient throughout the course of treatment, and **explain the regulations** in your state or jurisdiction regarding the provider's responsibility to report information to the health department.
- Convey through your actions and words the specific areas, such as DOT, that you and the health department team can assist in the co-management of the patient.
- Explain the absolute **necessity of DOT**, and emphasize to the provider the benefit of DOT to the patient. Daily contact with the patient through the provision of DOT will ensure that any problems the patient may experience are identified and addressed quickly. Patients frequently take their cues from their clinicians; enlist the provider's support in encouraging the patient to accept DOT.
- Explain the **infection control** practices required to keep office staff and other patients safe.
- Point the provider to resources that may be available to help manage the patient's co-morbid conditions, such as diabetes, malnutrition, and HIV.
- **Share this *Survival Guide* and a list of consulting resources** with the provider. Stress the importance of an expert in drug-resistant TB being involved throughout the course of treatment. In some areas, ongoing consultation with the regional experts is routine. See **Appendix 1, *Expert Resources for Drug-Resistant TB***.
- If the provider and staff have the infrastructure and resourcefulness to problem-solve with the patient (i.e., interfacing with insurance companies; seeking supplies of hard-to-get medications; making sure that the patient follows through on all monitoring; ordering and following through on detection of drug-resistance testing, blood levels, etc.), stay actively involved to ensure that **everything** gets done and is followed up appropriately.

- Touch base with the office staff regularly. Ensure essential monitoring tests are performed as indicated. Continue to offer yourself as a resource, problem-solver, and advocate. Anticipate staff needs, such as an audiologist who takes the patient's insurance or an interpreter whom the patient trusts.
- Ensure that the office staff has been appropriately evaluated if unprotected exposure to the patient has occurred.

**Reach an agreement about how and when important information (sputum and other laboratory results and radiographic results) will be shared between the private provider and public health agency.**

## Incarcerated patients

Special coordination of care is necessary when an MDR-TB patient is incarcerated at the time of diagnosis or during the course of treatment. Below are some areas for special attention:

- **Airborne infection isolation:** Patients will require isolation and may not be returned to the general population until they are considered non-infectious (see section: **Infection control** for suggested criteria). The need for respiratory isolation may require movement to a hospital or different facility and additional coordination to ensure all providers involved know the treatment plan. Occasionally, patients are in isolation for prolonged periods and may require physical and/or occupational therapy to prevent physical deconditioning and situational depression due to lack of movement and stimulation.
- **Adherence and DOT:** It will be important to educate facility staff regarding DOT; do not assume that medications are always observed when given in a correctional facility. Patients cannot be forced to take medications while incarcerated, and staff will need to work closely to address side effects and potential barriers to adherence.
- **Inmate movement:** During the long course of treatment, patients may move to different facilities or be paroled to the community. To ensure a patient is not moved without the awareness of medical staff, a stop sign or letter can be placed in the inmate's record indicating the need to ensure continuity of TB care. For a TB patient who is likely to move, enrollment in TBNet is strongly encouraged to ensure interruptions in treatment are minimized, appropriate follow-up and transfer of care occurs, and outcomes are reported.
- **Coordination of care:** The local TB program should be closely involved with the management of MDR-TB treatment and may also enlist an MDR-TB expert to provide consultation. The case manager should maintain regular communication with the facility's nursing and clinical staff and be proactive in coordinating care when an inmate will be moved to another facility (e.g., schedule a teleconference with staff from both facilities to review the care plan). Other key members to involve in the coordination of care include the facility pharmacist, state correctional medical officers, and the facility administrator.
- **Federal custody:** Give special consideration to MDR-TB patients who are in federal custody or who may transfer to the custody of a federal law enforcement agency. For patients who are diagnosed with MDR-TB while incarcerated or detained, health department staff should verify which agency has legal custody.

Health department staff should communicate with the respective law enforcement agency's health service staff to coordinate continuity of care and prepare and plan for possible transfer, release, or deportation. Transfers may occur to another jurisdiction and/or to the custody of a different law enforcement agency for reasons unrelated to health status. It is important to keep in mind that the law enforcement agency having legal custody may differ from the correctional or detention facility providing housing, security, and care for the prisoner, detainee, or inmate.

- **Deportation:** MDR-TB patients may be at risk for deportation if they are ordered removed by a federal immigration judge. Health department staff should ascertain whether the patient is in the custody of U.S. Immigration and Customs Enforcement (ICE), or if they have an ICE detainer and are scheduled to transfer to ICE custody upon completion of the sentence or resolution of criminal charges. Health department staff should promptly communicate with the ICE Health Service Corps, Public Health, Safety, and Preparedness Unit to coordinate case management and prepare for any possible outcome to the legal proceedings. TBNet enrollment should be verified to ensure continuity of care services for these patients. See **Resources** for contact information.

## Infection control

As noted in the WHO 2014 guide for programmatic management of drug-resistant TB, drug-resistant TB is similar in transmissibility to drug-susceptible TB and requires similar infection control strategies. In order to halt the transmission of *M. tuberculosis* complex, including drug-resistant TB, the correct diagnosis must first be considered, the appropriate treatment initiated, and appropriate infection control measures instituted. Infectious or potentially infectious drug-resistant TB patients should be housed within a negative pressure room in the hospital setting, or if they are outpatients, they should be separated from medically vulnerable family or friends.

When dealing with suspected or confirmed infectious drug-resistant TB, even greater emphasis should be placed on strict adherence to infection control standards as there is limited data on the efficacy of treatment of latent MDR-TB in exposed contacts. Unfortunately, infection control practices and isolation are a significant hardship for the patient and family and may unnecessarily perpetuate and exaggerate stigmatization of the patient with drug-resistant TB. When determining the duration of isolation, the safety of the public and the patient's family and contacts must be weighed against the mental health and morale of the patient as well as the resources required to isolate a patient.

- See **Resources** at the end of this chapter for publications that reflect current standard practices regarding TB and infection control. Local health jurisdictions are an important resource and may have specific guidelines.

### Assessing infectiousness and criteria for release from airborne infection isolation

The following information may be used to guide decisions in assessing infectiousness and determining when isolation may be discontinued:

- Studies have shown that most transmission of TB occurs before drug treatment has been initiated and that smear-positive cases transmit more efficiently than smear-negative cases. However, a 1999 molecular epidemiology study in San Francisco

documented TB transmission following exposure to AFB smear-negative, culture-positive TB cases accounting for 17% of secondary cases. Subsequent studies in the Netherlands and China substantiated this finding. See **Chapter 10, Contacts** for additional considerations regarding transmission and assessment for infectiousness.

- For drug-susceptible TB, a patient receiving TB treatment is deemed to be non-infectious when: he/she has taken and tolerated 2-3 weeks of an appropriate treatment regimen; he/she is clinically improving; and AFB smears have shown improvement if initially smear-positive. If initially AFB smear-negative, the patient can be deemed non-infectious after 5 days of effective treatment with clinical response. In a 2014 report from South Africa, MDR-TB patients became non-infectious once they were AFB smear-negative, started an effective regimen, and had evidence of clinical improvement.
- Because the transmission of MDR-TB has more serious potential consequences for contacts, **it is appropriate to be more cautious about returning MDR-TB patients back to their homes, schools, work sites, and congregate settings. All settings should be assessed by the local health department before determining whether a patient may safely return.**
  - **Take particular care when considering if patients can return to settings where there are young children, immunocompromised individuals, and people who have not previously been exposed to the patient.**
  - Some experts would consider MDR-TB patients **potentially** infectious as long as their sputum cultures remain positive. These experts recommend isolation while hospitalized and would not release MDR-TB patients to high-risk settings until sputum cultures are negative. See **Table 4 for an example of criteria used to determine when a patient with MDR-TB or suspected MDR-TB may be released from isolation to either a high-risk or low-risk setting.**



TABLE 4.

## Criteria for Release from Isolation to High and Lower Risk Settings\*

Patient Category	Setting	Criteria
<b>TB case (or suspect on treatment for TB) at increased risk for MDR-TB</b>	High or Lower risk	<ul style="list-style-type: none"> <li>Obtain direct NAAT, if available, for RIF and/or INH resistance.</li> <li>If direct NAAT not available, while phenotypic DST for RIF is pending, at the discretion of the local TB controller, either criteria for patients with known MDR-TB or criteria for patients not at increased risk of MDR-TB may be applied.</li> </ul>
<b>Known MDR-TB case</b>	High risk	<ul style="list-style-type: none"> <li>Three consecutive respiratory specimens collected on separate days, including at least one early AM or induced sputum, or BAL, are AFB smear negative, and no subsequent sputum specimen is AFB smear positive;</li> <li>At least 14 daily doses of treatment for MDR-TB taken and tolerated by DOT;</li> <li>Clinical improvement; and</li> <li>At least 2 consecutive negative sputum cultures without a subsequent positive culture.</li> </ul>
	Lower risk**	<ul style="list-style-type: none"> <li>Three consecutive sputum specimens collected on separate days are AFB smear negative;</li> <li>At least 14 daily doses of treatment for MDR-TB taken and tolerated by DOT; and</li> <li>Clinical improvement.</li> </ul>

### Definitions:

#### High Risk Setting

- A housing or work setting in which others will share air with the TB patient and which is characterized by 1 or more of the following factors:
  - A large number or high density of persons.
  - The presence of persons at high risk of progression to active TB disease (e.g., children < 5, persons with HIV infection)
  - The presence of persons who have not been previously exposed to the TB patient.

#### Lower Risk Setting

- A **residential** setting not characterized as high risk, and:
  - No other persons will share the air with the TB patient; OR
  - Other persons who will share the air with the TB patient are not at increased risk for progression to TB disease if infected; OR
  - All persons at increased risk of progression to TB disease if infected, including all children under the age of 5 years, who will share the air with the TB patient, have been previously exposed to the TB patient, have had a complete medical evaluation and have been started on therapy, including window period treatment for presumed LTBI (TB1), as appropriate.
- A **work** setting not characterized as high risk, and in which no contacts are known or reasonably expected to be at increased risk of progression to TB disease if infected

\*Adapted from CDPH/CTCA Joint Guidelines for the Assessment of Tuberculosis Patient Infectiousness and Placement into High and Lower Risk Settings 2009

\*\*A patient may be considered for placement in a lower risk setting without meeting these criteria if no previously unexposed persons will be present (see section: **Home isolation**)

## Home isolation

Many patients with drug-resistant TB do not require hospitalization and may be on home isolation at the start of treatment. Some patients may be hospitalized to initiate treatment and become ready for discharge prior to becoming non-infectious. A number of factors should be taken into account when considering whether home isolation is appropriate:

- Physical environment (is the home very small and crowded with little air flow?)
- Medical risks of household members (young children, immunocompromised?)
- Stability of household (relative likelihood that no new members will enter)
- Anticipated adherence by the patient
- Safety and protection of service providers in the home

While TB patients cannot be excluded from their families and homes indefinitely, every effort should be made to ensure the safety of contacts.

When caring for drug-resistant TB patients who are considered potentially infectious, healthcare and other service providers entering the home to deliver DOT and/or other healthcare services (e.g., patient interviews, home infusions) must comply with current infection control measures to prevent occupational exposure. For information that is essential to consider when preparing for the care of infectious TB patients in the home setting, consult with national (National Institute for Occupational Safety and Health [NIOSH]) and state occupational health and safety programs, your state TB program, or your RTMCC.

*Decisions about home isolation should be made in consultation with the local health officer / TB controller and experts in the care of drug-resistant TB.*

In some cases, home isolation will not be possible. In these cases, if resources permit, consider:

- Patients can sometimes be housed in a motel room which has an air supply that vents to the outdoors.
- A mobile home or trailer may be rented or purchased and used to house the patient until they are non-infectious.

## Transportation

Considerations for transporting the infectious drug-resistant TB patient:

- **Private car:** Have windows down, mask patient if possible, eat outdoors at stops.
- **Ambulance:** Identify an ambulance company that has vehicles with negative pressure and high efficiency particulate air (HEPA) filtration. Patients should wear surgical masks, and providers and drivers should wear N-95 masks.
- **Commercial airline flights:** WHO guidelines consider patients with MDR-TB to be infectious until their sputa are culture-negative, and forbids travel in public airplanes or other public transportation until their sputa are culture-negative (see **Resources**).
- **Air ambulance:** Contact the patient's insurance company, your hospital social worker or case manager, or your expert resources to identify an air ambulance company or private flight arrangements to safely transport your patient. WHO and International Air Transport Association have published guidelines regarding transporting potentially infectious tuberculosis patients by airline (see **Resources**).

# Drug supply management

## Drug availability

Many second-line TB medications are not regularly in stock at local pharmacies or wholesalers. If your local pharmacy does not carry the drug, ask them to order it and ask them how long it will take to get it. If a pharmacy or wholesaler states a drug is not available or “in stock,” additional steps can help determine if the drug is truly unavailable.

1. Check the U.S. Food and Drug Administration (FDA) Drug Shortage website, or the American Society of Health-System Pharmacists Drug Shortage website to see if a drug shortage has been reported (see **Resources**).
2. Ask the pharmacy or wholesaler to check with other distribution centers.
3. Call (or ask the pharmacy to call) the drug manufacturer directly and ask:
  - If there is stock
  - How the drug can be obtained (e.g. through wholesalers and/or directly from the manufacturer)
  - If the drug is on allocation that requires a special request (as has been the case for AK)
  - If the drug is short-dated (expiration date is imminent and wholesalers will not keep in stock and may require special agreement to release the drug)
  - If out of stock, anticipated date of availability

If **not available** from the pharmacy or manufacturer:

- Contact the TB nurse consultant at the state health department or the state TB controller; if your state TB program supplies TB medications, its central pharmacy may carry or have access to second-line drugs.
- Contact local hospitals to see if they have supply to share.
- Try to identify a patient in the area who has recently been taking the drug and see how that patient’s case manager obtained the drug.

Additionally, if the local pharmacy cannot obtain the drug in a timely fashion, call your local hospital or a neighboring TB clinic and ask if you can borrow a quantity of the drug.

## Drug shortages

Drug shortages have become increasingly common in the United States and most TB programs have been impacted by shortages of first- and second-line TB drugs. CDC has received reports of difficulty obtaining INH, RIF, streptomycin (SM), CS, ETA, AK, and CM.

Suggestions for managing drug supply and addressing drug shortages:

- If your state does not have a central pharmacy that stocks and distributes drugs used to treat drug-resistant TB, order and keep on hand a several-month supply of drugs to prevent treatment interruption due to supply shortages.
- If you are told a required drug is on **back order, unavailable, or out of stock**, report this immediately to your state TB control program and complete the *TB Drugs & Diagnostics Shortages Reporting Form* at the National TB Controllers Association website. The FDA is also a potential resource. See **Resources**.

TB drug supply can also be impacted by insurance company policies. Some insurance companies will limit the number of days or weeks a pharmacy can supply certain medications. Fluoroquinolones and macrolides in particular, may require special treatment authorization from the insurance company. Suggestions for addressing this issue include:

- Ask the pharmacy to help you anticipate any such restrictions on the patient's prescription plan.
- Write a letter to the insurer explaining the medical condition, duration of anticipated use of the drug, and need for that particular drug over another formulary drug to request authorization for prescription coverage. For most efficient processing, include the patient's name, date of birth, insurance ID and policy numbers, as well as the subscriber information.

### **Drug storage and safety**

- Most of the drugs used to treat drug-resistant TB can be stored at room temperature (59° to 86°F; 15 to 30°C); however, keep the following medications **refrigerated**:
  - **PASER granules**—store below 59°F (15°C); can also be stored in freezer
- Work with the agency providing parenteral medications to make sure the suspended forms do not exceed their safe shelf lives.
- Ensure safety of needle handling and disposal.

See **Chapter 5, Medication Fact Sheets**, for more details about each drug.

# Tool 1: Drug-O-Gram

## Drug-O-Gram

<b>SUMMARY DATE:</b>	<b>NAME:</b>	<b>DOB:</b>	<b>HEALTH DEPARTMENT:</b>	<b>TREATING PHYSICIAN:</b>	<b>FILE NO.:</b>
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### TREATMENT REGIMEN

Date	Wt.	INH	RIF	PZA	EMB	AK	CM	MFX	LFX	ETA	CS	PAS	LZD	Date	spec	sm/cult	Comments

### BACTERIOLOGY

### SUSCEPTIBILITY RESULTS

Date	Spec.	Lab	INH	RIF	PZA	EMB	SM	AK	CM	MFX	LFX	ETA	CS	PAS	LZD	RFB	BDQ	Reported	

Treatment Key: ● = DOT; ▲ = SAT  
Adapted from Los Angeles County TB Control Program Drug-O-Gram

# Tool 2: MDR-TB Monitoring Checklist\*

Patient Name: SAMPLE PATIENT Treatment Start Date: May 5, 2015 Treatment Regimen: EMB, Moxifloxacin, Amikacin, Linezolid, PAS

Activity	Month of Treatment																		
	Baseline	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Date	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
<b>CLINICAL MONITORING</b>																			
Sputum smear and culture <sup>1</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
CXR <sup>2</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Weight <sup>3</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Symptom review <sup>4</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
DST <sup>5</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>LAB MONITORING FOR TOXICITY / CO-MORBIDITIES</b>																			
CBC <sup>6</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Creatinine <sup>7</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
LFIs <sup>8</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
K+, Ca, Mg <sup>9,10</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Drug level <sup>10</sup>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
TSH <sup>11</sup>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
HIV <sup>12</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pregnancy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>MONITORING PROCEDURES</b>																			
Audiogram <sup>13</sup>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vestibular exam <sup>14</sup>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vision exam <sup>15</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Peripheral neuropathy <sup>16</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Arthralgias <sup>17</sup>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Depression <sup>18</sup>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
EKG <sup>19</sup>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
<b>*Important: Monitoring recommendations may change if treatment regimen or patient status changes. A box indicates monitoring activity is recommended. Check box when activity is completed.</b>																			
<ol style="list-style-type: none"> <li>Collect three AFB smear and culture specimens every 2 weeks until smear conversion, and then 2-3 specimens monthly until cultures have converted to negative. Once cultures have converted, obtain at least 1 specimen monthly throughout therapy.</li> <li>Obtain baseline CXR and monitor q 3 months during the first year and q 6 months in the second year of treatment.</li> <li>Monitor weight monthly and adjust medications as needed.</li> <li>Monitor for symptoms monthly.</li> <li>Obtain first- and second-line DST results at baseline. Repeat if patient on RIPE and remains culture positive prior to MDR-TB Rx, and again if patient fails to convert culture after 3 months on treatment.</li> <li>Obtain weekly for first month, then monthly for patients on linezolid.</li> <li>Obtain creatinine at baseline and monthly while patient is on an injectable agent.</li> <li>LFIs at baseline and then monthly while patient is on PZA, ethionamide or PAS.</li> <li>K+, Ca++, and Mg++ at baseline and monthly while patient is on an injectable agent.</li> <li>Therapeutic drug levels (TDM) should be obtained for patients receiving cycloserine after 2 weeks on therapy and if signs of toxicity develop. TDM may be obtained for other drugs as clinically indicated.</li> <li>Monitor TSH at baseline and every 3 months while patient is on ethionamide or PAS, and more frequently if symptoms or abnormalities.</li> <li>Obtain baseline HIV.</li> <li>Perform audiogram at baseline and monthly while patient is on an injectable agent.</li> <li>Perform vestibular exam at baseline and monthly while patient is on an injectable agent.</li> <li>Perform visual acuity plus color discrimination exams at baseline and monthly while patient is on ethambutol or linezolid.</li> <li>Monitor for peripheral neuropathy at baseline and monthly while patient is on linezolid and as clinically indicated for patients on fluoroquinolones.</li> <li>Monitor for arthralgias at baseline and monthly while patient is on PZA or fluoroquinolone.</li> <li>Monitor for depression, agitation, or mental status change at baseline and monthly while patient on cycloserine.</li> <li>Obtain EKG at baseline and at least 2, 12, and 24 weeks for patients on bedaquiline and at baseline and after treatment start for patients on fluoroquinolones as clinically indicated.</li> </ol>																			

Adapted from a checklist developed by the California Department of Public Health TB Control Branch, MDR-TB Service





# Tool 4: Laboratory Flow Sheet

	<b>DATE:</b>								
<b>HEME</b>	WBC								
	Hgb/Hct								
	Platelets								
<b>Chemistry</b>	Na+								
	K+								
	Cl-								
	CO <sub>2</sub>								
	Ca <sup>++</sup>								
	Mg <sup>++</sup>								
	Total Bili								
	Glucose								
	BUN								
	Creatinine								
	Uric Acid								
	Alk Phos								
	AST (SGOT)								
	ALT (SGPT)								
	T. Protein								
	Albumin								
<b>ABG</b>	PH								
	PaO <sub>2</sub>								
	PaCO <sub>2</sub>								
	HCO <sub>3</sub>								
	O <sub>2</sub> Sat								
<b>Urine</b>	Spec. Gravity								
	pH								
	Ketone								
	Glucose								
	Protein								
	Heme								
	Cr Clearance								
<b>Other</b>	TSH								
	PT/PTT								
	HgbA1C								
	CD4								
	Viral Load								
	Pregnancy								
<b>Drug Levels</b>									

Revised September 2015. Adapted from a laboratory flow sheet developed by the Los Angeles County TB Control Program.

MONITORING & CASE MANAGEMENT

# Tool 5: Vision Screening Flow Sheet

Visual acuity chart used (type and distance e.g., 10 or 20 foot): \_\_\_\_\_

Color discrimination tool used (type and number of plates if applicable): \_\_\_\_\_

BASELINE RESULT						
Date	VISUAL ACUITY		COLOR VISION		Performed by (signature)	Comment or action
	Right eye	Left eye	Right eye	Left eye		
	___ / ___	___ / ___				

MONTHLY MONITORING						
Date	VISUAL ACUITY		COLOR VISION		Performed by (signature)	Comment or action
	Right eye	Left eye	Right eye	Left eye		
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
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	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				
	___ / ___	___ / ___				

**NOTE:** If changes from baseline noted during monthly screening, inform treating clinician and refer for further evaluation.

Adapted from the Oregon Health Authority TB Program Visual Acuity and Test for Color Discrimination form

MONITORING & CASE MANAGEMENT

# Tool 6: Hearing and Vestibular Screening Flow Sheet

Date	Change in hearing, ringing or fullness in ears?	Dizzy, weak or unsteady?	Romberg	Walking	Heel-to-Toe Walk	Audiogram		Signature	Comment/Action
						Left	Right		
Baseline	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		
	Left ear: Y / N Right ear: Y / N	Yes / No	Normal Loss of balance	OK Weaves Staggers	Does well Jerky Hesitates Sways	WNL Abn Stable	WNL Abn Stable		

**NOTE:** If changes from baseline noted during monthly screening, inform treating clinician and refer for further evaluation.

Adapted from the Texas Center for Infectious Disease Hearing/Vision/Vestibular Report

MONITORING & CASE MANAGEMENT

# Resources

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## MONITORING THROUGHOUT TREATMENT

### Screening for depression and psychosis

*Beck Depression Inventory* (available in English and in Spanish)  
Harcourt Assessment, San Antonio, TX; <http://www.pearsonclinical.com/psychology/products/100000159/beck-depression-inventoryii-bdi-ii.html>

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*Personal Health Questionnaire Depression Scale* (PHQ-9)  
[http://cqaimh.org/pdf/tool\\_phq9.pdf](http://cqaimh.org/pdf/tool_phq9.pdf)

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*Zung Self-Rating Depression Scale*  
<http://healthnet.umassmed.edu/mhealth/ZungSelfRatedDepressionScale.pdf>

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*Mental Health Assessment Tool*—Heartland National Tuberculosis Center (2013)  
[http://www.heartlandntbc.org/assets/products/mental\\_health\\_screening\\_tool.pdf](http://www.heartlandntbc.org/assets/products/mental_health_screening_tool.pdf)

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*Inventory of Depressive Symptomatology (IDS) and Quick Inventory of Depressive Symptomatology (QIDS)*  
<http://www.ids-qids.org/>

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*Nursing protocol for preventing psychiatric adverse events associated with cycloserine*—Utah Department of Health (2010)  
[http://health.utah.gov/epi/diseases/TB/guidelines/nursing\\_protocol.pdf](http://health.utah.gov/epi/diseases/TB/guidelines/nursing_protocol.pdf)

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## PATIENT-CENTERED CARE AND ENSURING ADHERENCE TO TREATMENT

### Providing the injectable agent

*Administration of Amikacin Injection*, Heartland National TB Center  
[http://www.heartlandntbc.org/assets/products/administration\\_of\\_amikacin\\_injection.pdf](http://www.heartlandntbc.org/assets/products/administration_of_amikacin_injection.pdf)

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*Administration of Capreomycin Injection*, Heartland National TB Center  
[http://www.heartlandntbc.org/assets/products/administration\\_of\\_capreomycin\\_injection.pdf](http://www.heartlandntbc.org/assets/products/administration_of_capreomycin_injection.pdf)

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Capreomycin package insert:  
[http://www.akorn.com/documents/catalog/package\\_inserts/17478-080-50.pdf](http://www.akorn.com/documents/catalog/package_inserts/17478-080-50.pdf)

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*Outpatient infusion therapy for MDR-TB: A practical guide* (2004) New Jersey Medical School National Tuberculosis Center.  
<http://globaltb.njms.rutgers.edu/downloads/products/InfusionTherapy.pdf>

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## Patient Education

For patient information sheets in multiple languages on some of the second-line anti-TB medications (CFZ, ETA, PAS, levofloxacin, MFX, pyridoxine) see British Columbia Centre for Disease Control website:

<http://www.bccdc.ca/health-info/diseases-conditions/tuberculosis/more-resources>

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For a patient education flip chart, see:

<https://drtbnetwork.org/mdr-tb-patient-education-flipchart>

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## Patient Disclosure/Consent Examples

*Disclosure and consent for second-line drug therapy for treatment of TB disease:*

Texas Department of State Health Services (2007)

[www.dshs.state.tx.us/idcu/investigation/forms/TB-411.pdf](http://www.dshs.state.tx.us/idcu/investigation/forms/TB-411.pdf)

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*Consent for treatment of TB (2nd-line medications)*

[http://health.utah.gov/epi/diseases/TB/forms/atbd/consent\\_secondline.pdf](http://health.utah.gov/epi/diseases/TB/forms/atbd/consent_secondline.pdf)

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## Economic Support (Health Care Coverage, Incentives and Enablers, Homeless)

National Immigration Law Center: [www.nilc.org](http://www.nilc.org)

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Centers for Disease Control and Prevention. CDC's *Self-Study Module 6: Managing Tuberculosis Patients and Improving Adherence* has section on incentives and enablers.

<http://www.cdc.gov/tb/education/ssmodules/pdfs/module6v2.pdf>

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*Homelessness and TB Toolkit*, Curry International Tuberculosis Center

<http://www.currytbcenter.ucsf.edu/homelessnessandtbtoolkit/index.html>

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## CONTINUITY OF CARE

### Interjurisdictional Transfers

Centers for Disease Control and Prevention: Process for international notification of TB cases

<http://www.cdc.gov/tb/programs/international/default.htm>

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CureTB: 619-542-4013 [http://www.sandiegocounty.gov/hhsa/programs/phs/cure\\_tb/](http://www.sandiegocounty.gov/hhsa/programs/phs/cure_tb/)

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TBNet: 512-327-2017 <http://www.migrantclinician.org/services/network/tbnet.html>

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### Incarcerated Patients

ICE Health Service Corps, Public Health, Safety, and Preparedness Unit: 202-732-4542 or 202-732-3467

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*Tuberculosis Case Management for Undocumented and Deportable Inmates/Prisoners/ Detainees in Federal Custody.* Available at: [http://tbcontrollers.org/docs/corrections/Federal\\_TBCaseMgmt\\_for\\_Undoc-Deport\\_Corrections\\_v3\\_08-12-2014.pdf](http://tbcontrollers.org/docs/corrections/Federal_TBCaseMgmt_for_Undoc-Deport_Corrections_v3_08-12-2014.pdf)

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## INFECTION CONTROL

CDC's *Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care Settings*, MMWR 2005; 54 (No. RR-17), available at: [www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5417a1.htm)

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Curry International Tuberculosis Center, 2011: *Tuberculosis Infection Control: A Practical Manual for Preventing TB* <http://www.currytbcenter.ucsf.edu/products/view/tuberculosis-infection-control-practical-manual-preventing-tb-printed-book>

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### Transportation – Commercial Airline Flights

World Health Organization. *Tuberculosis and air travel: guidelines for prevention and control; 3rd edition.* [http://www.who.int/tb/publications/2008/WHO\\_HTM\\_TB\\_2008.399\\_eng.pdf](http://www.who.int/tb/publications/2008/WHO_HTM_TB_2008.399_eng.pdf).

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International Air Transport Association. *Suspected communicable disease: General guidelines for cabin crew.* March 2015. <http://www.iata.org/whatwedo/safety/health/documents/health-guidelines-cabin-crew-2011.pdf>.

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## DRUG SUPPLY MANAGEMENT

U.S. Food and Drug Administration Drug Shortage website: <http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>

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American Society of Health-System Pharmacists Drug Shortage website: <http://www.ashp.org/menu/DrugShortages.aspxto>

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*TB Drugs & Diagnostics Shortages Reporting Form* at the National TB Controllers Association website: <http://www.tbcontrollers.org/>.

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Accessibility of all websites verified October 10, 2015.

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