**TREATMENT OF TUBERCULOSIS:**

**Standard Therapy for Active Disease in Adults and Adolescents, 2009**

- **Antituberculosis Drugs:** First-Line Medications – Standard Therapy for Active Disease in Adults & Adolescents

**Dosage and Administration:**

- Use three drugs initially for at least 2 months, then use two drugs for an additional 4 months.

**Adjunctive Treatments:**

- Exercise, nutritional therapy, and other supportive measures are important.

**Adverse Effects & Monitoring Comments:**

- Neutropenia, mild CNS effects, drug interactions, hepatitis, rash, peripheral neuropathy, discoloration of bodily fluids, drug interactions due to other drugs.

**Drug Interactions:**

- Significant interactions with certain HIV medications, methadone, oral contraceptives.

**Contraindications:**

- Drug intolerance, allergy, severe immunologic reactions, orange discoloration of bodily fluids.

**Precautions:**

- Use in conjunction with RIF for treatment of LTBI; tests, and questioning each month.

**Hepatitis Risk:**

- Increases with age, alcohol use, concurrent use of other hepatotoxic drugs.

**Supplementation:**

- Pyridoxine in patients with nutritional deficiency, medical conditions associated with peripheral neuropathy (i.e., diabetes, chronic renal insufficiency).

**Creatinine Clearance:**

- Adjust dose or dosing interval when creatinine clearance is <30 ml/minute.

**Other Medications:**

- Used as a substitute for RIF if patient demonstrates RIF intolerance or is taking drugs that have unacceptable interactions with RIF.

**Questions & Answers:**

- Patients should be encouraged to return to the health department to complete the course of therapy.

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**NOTE:** This card is not intended as a complete reference for treatment of TB.
TREATMENT OF TUBERCULOSIS: Standard Therapy for Active Disease in Adults and Adolescents 2009

### Drug Card

<table>
<thead>
<tr>
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<th>Route</th>
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<tbody>
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**Adverse Reactions**
- Nausea, vomiting, abdominal pain, hepatitis, liver toxicity, jaundice, DI symptoms, rash, optic neuritis, hyperuricemia, gout

**Interactions**
- Avoid concomitant use of INH, RIF, EMB, PZA, and Rifapentine (RPT) due to increased risk of hepatotoxicity. Monitor LFTs and baseline uric acid before starting therapy.

**Monitoring**
- LFTs should be monitored monthly and when symptoms occur.
- Baseline visual acuity tests, color discrimination tests, and questioning each month are recommended.

**Follow-up**
- Rifapentine should be continued until treatment completion program or private provider must not only prescribe an appropriate regimen, but also ensure adherence until treatment completion.

### Treatment of Tuberculosis

1. **All patients** should undergo a drug susceptibility test on the initial regimen.
2. **Directly Observed Therapy (DOT)** is the international standard of care for all patients with TB disease and is essential for management of cases of multidrug-resistant TB (MDR-TB).
3. **Patients** with TB should monitor their monthly monitoring sputum for AFB smear and culture, until negative.
4. **All patients** should be initially started on a 4-drug regimen of Isoniazid (INH) and Rifampin (RIF).
5. A **single drug** should never be added to a failing treatment regimen. Treatment of suspected drug-resistant TB should be based on medication history and drug susceptibility results.
6. Treatment regimens for pulmonary TB are also effective for treating extrapulmonary TB.

### Treatment Completion

- **Treatment completion program or private provider must not only prescribe an appropriate regimen, but also ensure adherence until treatment completion.**

### Treatment Monitoring

- **Patients** should be monitored for potential drug resistance and drug toxicities.

### Treatment Regimens

- **Based on medication history and drug susceptibility results,** treatment for MDR-TB should be based on the Official Joint Statement of the American Thoracic Society and Centers for Disease Control and Prevention.

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**DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS IN ADULTS**

**Definition Phase**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Initial Phase</th>
<th>Continuation Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RIF or INH</strong></td>
<td><strong>7 days/wk for 14 doses (2 weeks)</strong></td>
<td><strong>INH/RIF 3x/wk for 54 doses (18 weeks)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>INH/RIF c 2x/wk for 36 doses (18 weeks)</strong></td>
<td><strong>7 8 (26 weeks)</strong></td>
</tr>
<tr>
<td><strong>PZA</strong></td>
<td><strong>5 days/wk for 40 doses (8 weeks)</strong></td>
<td><strong>90 doses (18 weeks)</strong></td>
</tr>
<tr>
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<td><strong>92-7 6 (26 weeks)</strong></td>
</tr>
<tr>
<td></td>
<td><strong>EMB 5 days/wk for 10 doses (2 weeks)</strong> then <strong>2x/wk for 12 doses (6 weeks)</strong></td>
<td></td>
</tr>
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### Default Phase

<table>
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<tr>
<th>Regimen</th>
<th>Interval &amp; Doses</th>
<th>Range of Total Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RIF</strong></td>
<td><strong>2-4 mg/kg daily or 600-5400 mg/week</strong></td>
<td><strong>12-108 months</strong></td>
</tr>
<tr>
<td><strong>INH</strong></td>
<td><strong>H, 30-40 mg/kg daily or 1800-2400 mg/week</strong></td>
<td><strong>12-108 months</strong></td>
</tr>
<tr>
<td><strong>RIF + INH</strong></td>
<td><strong>DCS</strong></td>
<td><strong>9-12 months</strong></td>
</tr>
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**Adjunct Antitubercular Agents**

- **Moxifloxacin (MOX):** PO 750-1500 mg/day
- **Levofloxacin (LEV):** PO 500-750 mg/day
- **Azithromycin (AZM):** PO 500 mg/day
- **Ethambutol (EMB):** PO 25 mg/kg/day
- **Cycloserine (CS):** PO 1-2 g/day
- **Prothionamide (PT):** PO 2-3 g/day
- **Streptomycin (SM):** IM 1-2 g/mo
- **Pentamidine (PTM):** PO 5 mg/kg/day
- **Piperacillin (PAP):** PO 2-3 g/day

**Monitoring:**

- **Baseline hearing & serum creatinine measurement.** Monthly renal function assessment and questioning regarding auditory or vestibular symptoms.
- **Baseline hepatic enzymes and thyroid function.** Baseline LFTs recommended in all patients. For patients with pre-existing liver disease or who develop abnormal liver function that does not require discontinuation of the drug, LFTs should be measured monthly & when symptoms occur.
- **Monthly renal function assessment and questioning regarding auditory or vestibular symptoms.**
- **Baseline hearing & serum creatinine measurement.** Baseline LFTs recommended in all patients. For patients with pre-existing liver disease or who develop abnormal liver function that does not require discontinuation of the drug, LFTs should be measured monthly & when symptoms occur.

**Adverse Reactions:**

- **GI intolerance, headache, dizziness, rash, vaginitis,**
- **Neuropsychiatric status assessed monthly.** Auditory, vestibular, and renal toxicity, drug interactions, hypersensitivity.
- **Ototoxicity (hearing loss or vestibular disease) or who develop abnormal liver function that does not require discontinuation of the drug, LFTs should be measured monthly & when symptoms occur.**
- **Baseline hearing & serum creatinine measurement.** Monthly renal function assessment and questioning regarding auditory or vestibular symptoms.
- **Baseline hepatic enzymes and thyroid function.** Baseline LFTs recommended in all patients. For patients with pre-existing liver disease or who develop abnormal liver function that does not require discontinuation of the drug, LFTs should be measured monthly & when symptoms occur.

**Drug Interactions:**

- **Avoid or reduce dose in adults over age 59 (10 mg/kg daily with a maximum dose of 750 mg).**
- **Monitor cardiac patients for sodium load. Doubling of prothrombin time lessened with use of SM.**
- **Renal insufficiency. Should not be used with aminoglycosides.**
- **Use cautiously in patients with renal insufficiency. Pyridoxine may decrease CNS effects. Avoid sunlight. Consider dosing at mealtime.**
- **Drug serum monitoring.**
- **Cross resistance with Ciprofloxacin and Ofloxacin.**
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**Comments:**

- **Patients with drug-resistant TB should be placed on directly observed therapy (DOT).** Second-line drugs are not intended for intermittent use and should be given on a daily basis. Exercise extreme caution when using these drugs during pregnancy due to known and unknown risk to the fetus.
- **Never add a single drug to a failing regimen.**
- **Baseline hearing & serum creatinine measurement.** Monthly renal function assessment and questioning regarding auditory or vestibular symptoms.
- **Drug serum monitoring.**

**DISCLAIMER:** Discontinuation, Substitution, Substitution, & Substitution are not considered standard drugs, but are used as alternatives to the standard therapy against drug-resistant tuberculosis. (Not stated in ATS/CDC/IDSA treatment statement).
**RECOMMENDATIONS FOR ADMISSION TO A PMTCT PROGRAM**

- **Intravenous (IV) therapy**
- **Contraindications**
  - **Pregnancy**
  - **Lactation**
  - **Renal insufficiency**
  - **Hypersensitivity to the drug**
  - **Children under 12 years of age**
  - **Patients with severe hepatic disease**
  - **Patients with severe renal disease**
  - **Patients with severe cardiac disease**
  - **Patients with severe pulmonary disease**

**DRUG REGIMENS FOR CULTURE-POSITIVE PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS IN ADULTS**

**Induction Phase**

<table>
<thead>
<tr>
<th>Drug</th>
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<th>Routes</th>
<th>Monitoring</th>
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<tbody>
<tr>
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<td>7 days/week for 14 doses (2 weeks)</td>
<td>INH/RIF</td>
<td>Baseline hearing &amp; serum creatinine measurement. Monthly renal function assessment and questioning regarding auditory or vestibular symptoms.</td>
<td>May cause hypothyroid condition if used with ETA. Monitor cardiac patients for sodium load. Double prothrombin time lessened with use of SM. Avoid or reduce dose in adults over age 59 (10 mg/kg daily with maximum dose of 750 mg). Decrease dose with renal insufficiency. Use cautiously in patients with renal insufficiency. Pyridoxine may decrease CNS effects. Avoid sunlight. Consider reducing dosage in patients with creatinine clearance of &lt;30 mL/min; start with low dosage and increase as tolerated. To reduce GI upset, give in divided dose. May cause hypothyroid condition, especially if used with PAS. Cross resistance with Ciprofloxacin and Ofloxacin. <strong>Cross resistance with Ciprofloxacin and Ofloxacin.</strong></td>
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<td>Baseline and monthly auditory and renal function as well as serum K+ and Mg+ levels.</td>
<td>May cause hypothyroid condition if used with ETA. Monitor cardiac patients for sodium load. Double prothrombin time lessened with use of SM. Avoid or reduce dose in adults over age 59 (10 mg/kg daily with maximum dose of 750 mg). Decrease dose with renal insufficiency. Use cautiously in patients with renal insufficiency. Pyridoxine may decrease CNS effects. Avoid sunlight. Consider reducing dosage in patients with creatinine clearance of &lt;30 mL/min; start with low dosage and increase as tolerated. To reduce GI upset, give in divided dose. May cause hypothyroid condition, especially if used with PAS. Cross resistance with Ciprofloxacin and Ofloxacin. <strong>Cross resistance with Ciprofloxacin and Ofloxacin.</strong></td>
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**Continuation Phase**

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**Notes:**

- The drug regimen should be administered daily, unless otherwise specified.
- **Doses:** The doses are based on the body weight of the patient and should be adjusted accordingly. The dose should be increased by the amount of body weight above 75 kg. The dose should be decreased by the amount of body weight below 45 kg.
- **Frequency:** The frequency of administration should be based on the patient's response to treatment, tolerability, and drug concentration in the serum.