# Treatment of Drug Susceptible Tuberculosis (TB) Disease in Children and Adolescents

2023

This card provides an overview of the treatment of drug-susceptible TB disease in children and adolescents and is not intended as a complete reference. Consult AAP and CDC guidelines for complete information on treatment of TB disease.

Content based on American Academy of Pediatrics (AAP) guidelines with consideration for Centers for Disease Control and Prevention (CDC) guidelines, expert input, and practical applications (see references)

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## Treatment Information

- Consultation with a TB specialist is recommended for the management of TB disease in children, especially in infants, children with confirmed or suspected drug-resistant TB, children with immunosuppression (including HIV infection), extrapulmonary TB (except peripheral lymph node TB), drug intolerance, suspected or confirmed non-adherence to treatment, or treatment interruptions.
- All cases of confirmed and suspected TB should be reported to state or local health departments; contact and source case investigations should be performed. TB prevention and care requires collaboration between clinical providers and public health programs.
- In addition to the standard 6-month regimen of rifampin (RIF), isoniazid (INH), pyrazinamide (PZA), and ethambutol (EMB), shorter regimens are now available for treatment of TB disease in *some* children:
  - Aged ≥3 months with non-severe TB (see regimen table): 4-month regimen of daily RIF, INH, PZA, and EMB for 2 months followed by INH and RIF daily for 2 months
  - Aged ≥12 years and body weight ≥40 kg: 4-month regimen of daily INH, rifapentine, moxifloxacin, and PZA for 8 weeks followed by INH, rifapentine, and moxifloxacin daily for 9 weeks
- Consult AAP and CDC for most recent information, as updated guidance may be available; as always, providers should use clinical judgement for management of individual patients.

## Special Circumstances

- Children with HIV/immunosuppression: The clinical manifestations and radiographic appearance of TB disease tend to be similar to those in immunocompetent children, but the manifestations can be more severe, unusual, and more often include extrapulmonary involvement of multiple organs in those with severe immunosuppression. Therapy should always include at least 4 drugs administered daily via DOT for at least the first 2 months and should be continued for at least 6 months (except in cases of non-severe pulmonary disease) and may require adjustment of ART due to medication interactions. Consultation with a specialist who has experience in managing patients with TB who are living with HIV infection is strongly advised.
- Drug-resistant TB: Consult an expert if drug-resistant TB is suspected or confirmed.

## Administration & Monitoring

- Directly Observed Therapy (DOT) is strongly recommended for children with TB disease; intermittent therapy MUST be provided by DOT.
- Medications should be given concurrently to prevent drug resistance, enhance adherence, and achieve optimum drug levels.
- Adjust weight-based dosages as weight changes.
- Careful monthly monitoring of clinical and bacteriologic response to therapy is important; regular physician-patient contact to assess drug adherence, efficacy, and adverse effects is integral to management of TB disease; DOT visits also allow opportunities for checking on well-being and treatment tolerance.
- Hepatotoxic effects in children are rare and routine determination of serum aminotransferase concentrations is not recommended in most cases of TB disease unless the child develops symptoms suggestive of hepatotoxicity (e.g., anorexia, nausea, vomiting, abdominal pain, jaundice).
  - Monitoring is also recommended in individuals with underlying or suspected hepatic or biliary disease, use of concomitant hepatotoxic drugs (e.g., anti-convulsants, HIV agents, or acetaminophen), HIV infection, regular use of alcohol or injection drugs, or when pregnant or <3 months postpartum.
  - Monthly clinical evaluation to observe for signs or symptoms of hepatitis and other adverse effects of drug therapy is appropriate follow up in most cases.
- Chest radiographs should be obtained after 2 months of therapy to evaluate response in children with pulmonary disease and symptom improvement.
  - Though complete resolution of radiographic abnormalities is not expected within 2 months of therapy for children with pulmonary TB, interval improvement in interstitial infiltrates is expected. Pleural effusions might take longer to resolve completely.
  - Any child with new wheezing on treatment should have a repeat CXR to assess for lymphadenopathy or bronchial obstruction.
- Administering medications for an extended time can be challenging, especially for very young children. Strategies include crushing pills or opening capsules and mixing with a small amount of soft appealing food (e.g., mashed banana or sugar-free applesauce, pudding, or yogurt). Dissolve crushed pills in a few drops of warm water to create a slurry before mixing with food and use the smallest amount of food possible to ensure that the entire dose is consumed. Give medication promptly after mixing with food.

## Regimens for Presumed or Known Drug-Susceptible TB in Children & Adolescents[a]

(Treatment includes an intensive and continuation phase)

### Non-Severe TB

**Pulmonary TB which is:**

- Confined to one lobe with no cavities, **and**
- No signs of miliary TB, **and**
- No complex pleural effusion, **and**
- No clinically significant airway obstruction

**OR**

- Isolated intrathoracic adenopathy

**OR**

- Peripheral lymph node TB without lung involvement

| Criteria | Intensive Phase | + | Continuation Phase |
|---|---|---|---|
| Children ≥ 3 months: | 8 weeks of daily RIF, INH, PZA, and EMB[b] (RIPE) | + | 8 weeks of daily INH and RIF |
| Alternative regimen for children ≥12 years and body weight ≥40 kg | 8 weeks of daily INH, rifapentine, moxifloxacin, and PZA | + | 9 weeks of daily INH, rifapentine, and moxifloxacin |

**Comments:**

- Medication should be administered daily (DOT is strongly preferred).
- At a minimum, chest X-ray is required for individuals being evaluated for tuberculosis.

### Severe Pulmonary TB

TB that does NOT meet the above criteria for use of a 4-month RIPE regimen

**OR**

**Extrapulmonary TB** (other than TB meningitis or peripheral lymph node TB without lung involvement)

| Criteria | Intensive Phase | + | Continuation Phase |
|---|---|---|---|
| Children and adolescents | 8 weeks of RIF, INH, PZA, and EMB[b] (RIPE) daily or 3 times per week[c] | + | 18 weeks of INH and RIF daily or 3 times per week[c] |
| Alternative regimen for children ≥12 years and body weight ≥40 kg | 8 weeks of daily INH, rifapentine, moxifloxacin, and PZA | + | 9 weeks of daily INH, rifapentine, and moxifloxacin |

**Comments:**

- Extend 6-month RIPE regimen to at least 9 months if the initial chest radiograph shows one or more cavity and/or sputum culture remains positive after 2 months of therapy (expert consultation is strongly recommended).
- Treatment may be extended for miliary or bone and joint TB.
- Adjuvant treatment with corticosteroids can be considered for children with pleural and pericardial effusions, severe miliary disease, endobronchial disease, and abdominal TB.

### TB Meningitis (CNS-TB)

| Criteria | Intensive Phase | + | Continuation Phase |
|---|---|---|---|
| Children and adolescents | 8 weeks of daily INH, RIF, PZA, and ethionamide (if possible) and/or a fluoroquinolone[d,e] | + | 7-10 months of INH and RIF once a day |

**Comments:**

- Expert consultation is strongly recommended.
- Increase RIF dose to 20-30 mg/kg/day to ensure adequate CNS penetration.
- Adjuvant treatment with corticosteroids should be strongly considered.

### Drug-Resistant TB

Consult an expert if drug-resistant TB is suspected or confirmed.

a. Duration of therapy may be longer in children with HIV and additional drugs and dosing intervals may be indicated.
b. Some experts administer 3 drugs (INH, RIF, and PZA) as the initial regimen if a presumed source person has been identified with known pan-susceptible *M. tb* (or has no risk factors for DR-TB) **and** the child is HIV negative.
c. Medications should be administered daily for the first 2 weeks to 2 months of treatment and then may be administered daily or 3 times per week by DOT; however, most experts prefer daily therapy. DOT is required for intermittent regimens. Twice weekly is acceptable in rare cases if resources for DOT are limited. Intermittent therapy is **not** recommended in those with HIV.
d. Levofloxacin or moxifloxacin; parenteral capreomycin or aminoglycosides (streptomycin, kanamycin, or amikacin) could be used instead.
e. When susceptibility to first-line drugs is established, ethionamide, fluoroquinolone, and/or aminoglycoside (or capreomycin) can be discontinued.

## Common Medications for Presumed or Known Drug-Susceptible TB Disease in Children & Adolescents

Medications for TB disease are generally safe and well tolerated in children and adverse drug reactions (ADRs) are rare. In case of possible severe ADRs, discontinue treatment and provide supportive medical care as indicated.

| Drug | Formulation | Daily Dosage[a] | Most Common ADRs | Comments |
|---|---|---|---|---|
| Isoniazid **INH**: PO | 100 or 300 mg scored tablets[b] | 10 mg/kg<br>Range: 10-15 mg/kg[c]<br>Max: 300 mg | Mild hepatic enzyme elevation, hepatitis, peripheral neuritis, hypersensitivity | Supplement with pyridoxine (vitamin B6) up to 1-2 mg/kg/day, usually 25-50 mg/day (max 50 mg) in these circumstances: meat/milk deficient diets, nutritional deficiencies, HIV infection, exclusively breastfed infants, pregnant or breastfeeding adolescents, existing peripheral neuropathy / paresthesias (or if symptoms develop). |
| Rifampin **RIF**: PO | 150 or 300 mg capsules[c] | Range: 15-20 mg/kg[d]<br>Max: 600 mg | Orange discoloration of secretions or urine, staining of contact lenses, vomiting, hepatitis, influenza-like reaction, thrombocytopenia, pruritus; oral contraceptives may be ineffective | Decreases serum levels of many drugs. Significant interactions can occur with certain HIV medications. Rifabutin is an alternative for use with HIV medications; however, use in children has been limited. Educate patients about normal orange discoloration of bodily fluids. Permanent discoloration of hard contact lenses may occur; this is unlikely with disposable contact lenses. Instruct adolescents who use hormonal birth control to add, or switch to a barrier method. |
| Rifapentine **RPT**: PO | 150 mg tablets (blister pack) | Children ≥40 kg: 1200 mg | | |
| Pyrazinamide **PZA**: PO | 500 mg scored tablets | 35 mg/kg<br>Range: 30-40 mg/kg<br>Max: 2 g | Hepatotoxic effects, hyperuricemia, arthralgia, gastrointestinal (GI) tract upset, pruritus, rash | Use of PZA in pregnancy in the US is debated; it may be used on a case-by-case basis after risk/benefit conversation with the patient, if benefit outweighs risk. If PZA is omitted for any reason, treat with INH, RIF, and EMB for 9 months; consider expert consultation. |
| Ethambutol **EMB**: PO | 100 or 400 mg tablets | 20 mg/kg<br>Range: 15-25 mg/kg<br>Max: 1 g | Optic neuritis (usually reversible), decreased red-green color discrimination, GI tract disturbances, hypersensitivity | Baseline and monthly monitoring for visual acuity and color discrimination (Ishihara plates) is indicated. |
| Ethionamide: **ETH**: PO | 250 mg tablets | 15-20 mg/kg, given in 2-3 divided doses<br>Max: 1 g | GI tract disturbances, hepatotoxic effects, hypersensitivity reactions, hypothyroidism | Can be given at bedtime or with a main meal to reduce nausea. Clinicians experienced with using ethionamide suggest starting with 250 mg once daily and gradually increasing as tolerated. Serum concentrations may be useful in determining the appropriate dose. |
| Levofloxacin **LFX**: PO | Tablets: 250, 500, or 750 mg<br>Oral Solution: 25 mg/mL | Adults: 750-1000 mg (once daily)<br>Children: 15-20 mg/kg<br>Max: 1 g | Hypersensitivity reactions; theoretical effect on growing cartilage, tendonitis, GI tract disturbances, cardiac disturbances, peripheral neuropathy, rash, headache, restlessness, confusion; can prolong QTc interval | Levofloxacin and moxifloxacin do not have an indication from the FDA for TB treatment and are not approved by the FDA for use in children <18 years of age but are commonly used and included in AAP and CDC recommendations; have risk/benefit conversation with the family. 400 mg dose of moxifloxacin is used in the alternative 4-month rifapentine-moxifloxacin regimen for children ≥12 years and body weight ≥40 kg. |
| Moxifloxacin **MFX**: PO | 400 mg tablets | Adults: 400 mg (once daily)<br>Children: 10 mg/kg (once daily)<br>Max: 400 mg | | |

a. Although intermittent dosing may be used for some regimens, many experts prefer daily dosing for treatment of TB disease in children. Intermittent treatment must be provided by DOT. Consult the AAP Red Book for additional information.

b. Although a liquid INH preparation is available and both INH and RIF can be compounded by a pharmacy, these preparations contain sorbitol, which can cause diarrhea, cramping, and abdominal pain and is generally not recommended; the technique of mixing crushed pills/capsule contents with a few drops of warm water and adding to a small amount of soft food the child likes is generally very successful and can be used in most children.

c. When INH dosage exceeding 10 mg/kg/day is used in combination with RIF, incidence of hepatotoxic effects may be increased.

d. Many experts recommend using a daily rifampin dose of 20-30 mg/kg/day for infants and toddlers and for serious forms of TB disease, such as meningitis and disseminated disease (e.g., miliary TB).

## References and Resources

Red Book: 2021–2024 Report of the Committee on Infectious Diseases, 32nd Edition. Updates to Tuberculosis. July 19, 2023: publications.aap.org/redbook/book/347/chapter-abstract/5757587/Tuberculosis

Interim Guidance: 4-Month Rifapentine-Moxifloxacin Regimen for the Treatment of Drug-Susceptible Pulmonary Tuberculosis — United States, 2022, CDC: cdc.gov/mmwr/volumes/71/wr/mm7108a1.htm?s_cid=mm7108a1_w

Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. 2016

- Highlights and access to full text: cdc.gov/tb/topic/treatment/guidelinehighlights.htm

**Consult CDC and AAP for up-to-date information as guidelines may change. Consultation is available from:**

- Your TB program: cdc.gov/tb/php/tb-programs/index.html
- Regional TB Centers of Excellence: cdc.gov/tb-programs/php/about/tb-coe.html

For additional resources, scan below or go to: globaltb.njms.rutgers.edu/

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