

Fixed-dose combinations for the treatment of TB in children

QUICK FACTS

- At least 1 million children become ill with tuberculosis (TB) each year. Children represent about 10-11% of all TB cases.
- In 2016, 253,000 children died of TB, among whom 52,000 were living with HIV.
- TB in children can be treated. Most children tolerate treatment very well.
- Simple, child-friendly fixed-dose formulations are easy to administer and match WHO dosage recommendations for first line treatment.
- Preventive treatment is highly effective in children exposed to TB.

TREATING TB IN CHILDREN

All children treated for TB should be registered with the National TB programme.

The following dosages of first-line anti-TB medicines should be used daily for the treatment of TB in children:

Isoniazid (H)	10 mg/kg (range 7–15 mg/kg)
Rifampicin (R)	15 mg/kg (range 10–20 mg/kg)
Pyrazinamide (Z)	35 mg/kg (range 30–40 mg/kg)
Ethambutol (E)	20 mg/kg (range 15–25 mg/kg)
As children approach a body weight of 25 kg, adult dosages can be used	

- First line treatment of drug-sensitive TB consists of a two-month intensive phase with isoniazid, rifampicin, pyrazinamide (and, depending on the setting and type of disease, ethambutol), followed by a continuation phase with isoniazid and rifampicin for at least four months. HIV-infected children with TB require antiretroviral therapy (ART) and co-trimoxazole preventive therapy (CPT) in addition to TB treatment.
- Preventive therapy is highly effective in children exposed to TB; 3-months daily rifampicin plus isoniazid may be offered as an alternative TB preventive treatment to the six-months Isoniazid monotherapy for both adults and children but they should be prescribed with caution to people living with HIV who are on ART because of potential drug-drug interactions.

- Support of the child, his/her parents and immediate family is vital to ensure the completion of treatment and a successful outcome. This may include nutritional, financial and counselling assistance.

SIMPLE, CHILD-FRIENDLY TB TREATMENT

Until recently, there was no appropriate first-line TB treatment designed for children. However, after sustained advocacy and new investment, now child-friendly formulations that do not need to be cut or crushed to achieve an appropriate dose are available, offering the opportunity to simplify and improve treatment for children everywhere.

The formulations were developed in line with the revised dosing published in the 2014 WHO Guidance on childhood TB through a project led by TB Alliance and WHO (Essential Medicines and Health Products department and the Global TB Programme), and funded by UNITAID and USAID.

The fixed-dose combinations (FDCs) are not new drugs, but rather improved formulations of currently used medicines recommended for the first line treatment of TB.

The FDCs are WHO prequalified, included in the 6th edition of the WHO Essential Medicines List for Children and recommended to replace previously used medicines for children weighing less than 25 kg.

BENEFITS OF CHILD-FRIENDLY TB FORMULATIONS

- **The right medicines in the right doses will increase adherence and save more lives.** This is an important step in improving treatment and child survival from TB, and slowing the spread of drug-resistant TB.
- **Simple TB medicines for children eases the TB burden on healthcare systems.** Using fixed-dose combinations for children eases procurement of TB medicines. Fewer pills will simplify ordering and storage, and facilitate scale-up of pediatric treatment.
- **Child-friendly medicines improve the daily lives of children and their families struggling with TB.** Six months is a long time to take medicine. But the availability of treatment that tastes good and is simple to provide will ease the daily struggles of children, parents, and caregivers alike.

ABOUT THE FIXED-DOSE COMBINATIONS FOR CHILDREN

The formulations available are :

For the intensive phase of TB treatment:

Rifampicin 75 mg + Isoniazid 50 mg +
Pyrazinamide 150mg

For the continuation phase of TB treatment:

Rifampicin 75mg + Isoniazid 50 mg

The following dosing table provides information on the number of daily tablets needed to reach the proper dosing, based on the child's weight:

Weight band	Numbers of tablets	
	Intensive phase: RHZ 75/50/150*	Continuation phase: RH 75/50
4-7 kg	1	1
8-11 kg	2	2
12-15 kg	3	3
16-24 kg	4	4
25+ kg	<i>Adult dosages recommended</i>	

*Ethambutol should be added in the intensive phase for children with extensive disease or living in settings where the prevalence of HIV or of isoniazid resistance is high

** Treatment of infants 0-3 months, or infants below 4 kg, should be undertaken by a clinician experienced in managing pediatric TB. If such expertise is not available, and TB has been definitively diagnosed or is strongly suspected, treatment with the standard drug regimen may be considered.

HOW CAN COUNTRIES ACCESS THE NEW FORMULATIONS

Countries can access the new formulations through the Global TB Drug Facility (GDF).

TB high burden countries can utilize the WHO Collaborative Procedure for fast track registration and can benefit from technical assistance for transitioning from the old to the new formulations.

OTHER PRODUCTS IN THE PIPELINE

Other products under development and likely to be available soon are:

- 100 mg ethambutol dispersible tablets;
- 100 mg isoniazid dispersible tablets (recommended for preventive treatment).

KEY REFERENCES

- Latent TB Infection. Updated and consolidated guidelines for programmatic management. WHO, 2018.
- Global TB Report 2017. World Health Organization, 2017.
- Guidance for national tuberculosis programmes on the management of tuberculosis in children: second edition. Geneva, World Health Organization, 2014.

INADEQUATE PEDIATRIC TREATMENT

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NOW AVAILABLE



INCORRECT DOSES



BROKEN PILLS







CRUSHED PILLS



BAD TASTE



CORRECT DOSES, DISSOLVABLE IN WATER, TASTES GOOD

For more information:

Global TB Programme, World Health Organization <http://www.who.int/tb/areas-of-work/children/>
TB Alliance www.tballiance.org/children