Appendix 10.2 Guidelines for TB treatment in young children using FDCs

(Taken from the 2014 WHO guidance document for national TB programmes on the management of TB in children)

To allow the currently available fixed-dose combinations (FDCs) to be used to achieve the desirable doses of anti-TB drugs for children, WHO has compiled the dosing charts in this annex as an interim measure, the following:

- ...ersible tablets should be used wherever possible, especially for children who ...lets.
- Regimen... in some cases may also require administration of single-component ph...
- These doses are for on... ...nd, wherever possible, avoid the need for splitting tablets.
- The recommended doses are generall... ...the dose ranges to minimise risk of toxicity.

These guidelines replace the interim recommendations publ... *Dosing instructions for the use of currently available fixed-dose combination TB med...*

Once children achieve a body weight of 25 kg, adult dosage recommendat... ...adult preparations used.

Weight band	Number of tablets		
	Intensive phase		Continuation phase
	RHZ (60/30/150)	E (100)	RH (60/30)
4–6 kg	1	1	1
7–10 kg	2	2	2
11–14 kg	3	2	3
15–19 kg	4	3	4
20–24 kg	5	4	5

Treatment of TB in young children (less than 25 kg) using currently available FDCs (RHZ 60/30/150), and dosages achieved per weight

Body weight	Number of tablets	Actual dosage (mg/kg) received when using number of tablets containing dosages listed for that weight band		
		Rifampicin 60 mg	Isoniazid 30 mg	Pyrazinamide 150 mg
4		15.0	7.5	37.5
5		12.0	6.0	30.0
6	1	10.0	5.0	25.0
7	2		8.6	42.9
8	2		7.5	37.5
9	2		6.7	33.3
10	2	12.0		30.0
11	3	16.4		40.9
12	3	15.0		37.5
13	3	13.9	6.9	34.6
14	3	12.9	6.4	
15	4	16.0	8.0	
16	4	15.0	7.5	
17	4	14.1	7.1	35.3
18	4	13.3	6.7	33.3
19	4	12.6	6.3	31.6
20	5	15.0	7.5	37.5
21	5	14.3	7.1	35.7
22	5	13.6	6.8	34.1
23	5	13.0	6.5	32.6
24	5	12.5	6.3	31.3

The content of this Appendix, 10.2, is outdated. Please see the two pages that follow this for the updated information

UPDATED VERSION OF APPENDIX 10.2

Guidelines for TB treatment in young children using new fixed-dose combinations

Taken from a World Health Organisation document, December 2016

QUICK FACTS:

- TB in children can be treated. Most children tolerate treatment very well
- Preventive therapy is highly effective in children exposed to TB
- Simple, child-friendly fixed-dose formulation are easy to administer and match WHO dosage recommendations for first line treatment

TREATING TB IN CHILDREN
All children treated for TB should be registered with the National TB program
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
- Isoniazid in the same dosage is recommended as preventive therapy over six months for children under the age of five as well as HIV-positive children of any age
- The support of the child, his/her parent and immediate family is vital to ensure the completion of treatment and a successful outcome. This may include nutritional, financial and counseling assistance

NEW HOPE FOR CHILDREN WITH TB
SIMPLE, CHILD-FRIENDLY TB TREATMENT NOW AVAILABLE
Until recently there has not been appropriate first-line TB treatment designed for children. However, after sustained advocacy and new investment, child-friendly formulations that do not need to be cut or crushed to achieve an appropriate dose are now 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 though a project led by TB Alliance and WHO (Essential Medicines and Health Products department and the Global TB Program) 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 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 ease 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 paediatric 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 now available are:
For the intensive phase of TB treatment:
Rifampicin 75 mg + isoniazid 50 mg + Pyrazinamide 150 mg

For the continuation phase of TB treatment:
Rifampicin 75 mg + isoniazid 50 mg

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

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

**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*

HOW CAN COUNTRIES ACCESS THE NEW FORMULATIONS

Following approval by a WHO Expert Review Panel in June 2015 countries can access the new formulations through the Global TB Drug Facility (GDF)
TB high burden countries can utilize the WHO Collaborative Procedure to fast track registration and can benefit from technical assistance for transitioning from the old to the new formulations.

OTHER PRODUCTS THAT ARE BEING MANUFACTURED BUT THERE MAY STILL BE ACCESS ISSUES

- 100 mg ethambutol dispersible tablets
- 100 mg isoniazid dispersible tablets (recommended for preventive therapy)

For access to these products, please discuss with staff dealing with supply.

KEY REFERENCES

- Global TB Report 2016 World Health Organisation, 2016
- Guidance for national tuberculosis programs on the management of tuberculosis in children: second edition. Geneva, WHO 2014

For more information:

Global TB Program, WHO, http://www.who.int/tb/areas-of-work/children

TB Alliance www.tballiance.org/children