Bedaquiline is much more widely available than delamanid for adults under programmatic conditions but nearly totally restricted from children due to lack of data [10]. Children with MDR-TB urgently need better treatment options. Expedited enrollment in Janssen's paediatric study of bedaquiline and the availability of the paediatric formulation for the IMPAACT network for its planned study of bedaquiline, including in HIV-positive children, would greatly advance treatment for paediatric MDR-TB. Children affected by MDR-TB, and those who care for them, have already waited too long.

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Paediatric study of bedaquiline is open but several years behind schedule, delaying access for children with MDR-TB <http://ow.ly/4mP8wm>

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New anti-tuberculosis drugs for special populations: a difficult-to-address issue

From the authors:

We read with interest correspondence from L. McKenna and L. Ruiz Mingote commenting on the editorial by Pontali *et al*. [1] “Bedaquiline and multidrug-resistant tuberculosis: a systematic and critical analysis of the evidence”. Their core message is the lack of availability of the new anti-tuberculosis (TB) drugs (*i.e.* bedaquiline and delamanid) for childhood TB. In particular, they advocate for rapid initiation of clinical trials in children after the proof of concept and dose-finding (IIa and IIb, respectively) studies carried out in adults.

Childhood TB, and specifically multidrug-resistant TB (MDR-TB) in this age group, has recently gained international relevance both in terms of numbers and difficult management [2–4]. The complicated bacteriological diagnosis in children is well known, so that often the paediatrician needs to rely on the

child's history of contact without having a drug susceptibility test to guide the regimen's design. In addition, chest radiography is often difficult to interpret, as are signs and symptoms [5, 6]. Furthermore, the lack of paediatric formulations for some of the drugs needed to treat MDR-TB in children creates an unacceptable "double standard", which needs to be tackled urgently [2].

There are several reasons behind the observed delay in making new drugs for children available. The paediatric population, as well as the elderly and pregnant or breastfeeding women, deserve *ad-hoc* experimental studies. Due to known (clinical, physiological, pharmacokinetic and pharmacodynamic) differences between adults and children, it is in fact not correct to translate "*tout court*" the findings obtained in adults to the paediatric population.

Specific clinical trials have to be designed to assess the efficacy, safety and tolerability of the new anti-TB drugs and regimens in special TB patient populations. As such trials are long and expensive, it is always difficult to identify companies or organisations willing to plan and implement them.

L. McKenna and L. Ruiz Mingote comment that a compromise should be found for children; when a drug or a regimen demonstrates its safety and efficacy in phase IIb experimental studies, then rapid translation into clinical practice can be activated [7]. It is, however, important to underline that phase IIa and IIb studies are often based on modest sample sizes and the random error related to the sampling procedures could affect a comprehensive evaluation of the efficacy, safety and tolerability profile of the new experimental drug or regimen.

Clinical and ethical considerations about the possible occurrence of rare and life-threatening adverse events need to be balanced against the potential benefits, taking into account the consequences for a new drug/regimen if something goes wrong (e.g. early retirement of the drug).

The *European Respiratory Journal* welcomes debate on the use of new drugs, particularly in the paediatric population. As we are facing more and more difficulties in the sustainability of the healthcare systems, even in high income countries (e.g. the UK) [8, 9], the discussion between policymakers (who look at the public health aspects) and clinicians (who have the dying child in front of them) is not always easy.

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Specific clinical trials are needed to assess efficacy, safety & tolerability of new anti-TB drugs for childhood TB <http://ow.ly/X9wl301VNiR>

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