

THE PRICE OF BEDAQUILINE

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INTRODUCTION

In December 2012, bedaquiline (Sirturo) became the first new tuberculosis (TB) drug from a new drug class to receive approval by the U.S. Food and Drug Administration (FDA) in 40 years. Since then, uptake of this important drug has been far below the global need. An August 2018 update to the World Health Organization (WHO) guidelines designated bedaquiline as a core component of treatment regimens for rifampicin-resistant and multidrug-resistant TB (RR-/MDR-TB).¹ As a result, even broader access to bedaquiline is now needed. Among barriers to bedaquiline access, affordability is a major concern, as the global donation program set up by the drug's sponsor, Janssen, a subsidiary of Johnson & Johnson, ends in March 2019.

THE PRICE OF BEDAQUILINE (AND ITS EVOLUTION)

Pre-donation program:

Janssen initially established a tiered pricing structure for bedaquiline. The price for a six-month course of bedaquiline was different for low-, middle-, and high-income countries (US\$900, \$3,000, and \$30,000, respectively).

Donation program:

In 2014, to facilitate the uptake of bedaquiline, Janssen and the U.S. Agency for International Development (USAID) set up a temporary global donation program. Under this donation program, most countries eligible to receive funding from the Global Fund could procure bedaquiline for free, via the Global Drug Facility (GDF). The program initially covered 30,000 treatment courses, all of which were claimed by July 2018. USAID and Janssen then made an additional 30,000 courses available until March 2019 (or when those 30,000 courses are claimed, whichever came first).

Post-donation program:

The price of bedaquiline is of serious concern in the post-donation era. There is a growing demand for bedaquiline that is stimulated by the latest WHO treatment guidelines, which reflect the substantial body of evidence that suggests that people who receive bedaquiline have higher rates of treatment success and lower rates of death than people who do not receive bedaquiline.^{2,3}

In July 2018, following its announced switch to bedaquiline-based, injection-free regimens for all people with RR-/MDR-TB, the South African Department of Health announced that it had negotiated with Janssen a price reduction of bedaquiline to \$400 per six-month course (\$67 per patient per month).⁴ Any country buying bedaquiline through the GDF now has access to this price as well. But this price is still too high, especially for programs to implement bedaquiline-based regimens for all people with

RR-/MDR-TB, consistent with revised WHO guidelines. Bedaquiline is just one of up to seven drugs that are necessary to compose a treatment regimen for RR-/MDR-TB. Many people need to take bedaquiline for more than six months (the duration at which it was initially studied by Janssen), which further extends the cost. A few simple comparisons make it clear that, at \$67 per month, bedaquiline is still excessively expensive:

- Currently, without including bedaquiline, the total cost of drugs for RR-/MDR-TB treatment regimens are already above the \$500 target set by Médecins Sans Frontières (MSF), ranging from \$571 to \$812.^{5,6}
- A full course of treatment for drug-sensitive TB costs just \$16–42 in drug costs.⁷
- At \$67 per patient per month, bedaquiline is more than double the cost of linezolid (\$29–42 per patient per month) and up to 22 times the cost of levofloxacin or moxifloxacin (\$3–9 per patient per month), the two other medicines the latest WHO treatment guidelines recommend programs use to form the core backbone of treatment regimens for RR-/MDR-TB.⁸
- Researchers from the University of Liverpool have calculated that bedaquiline could be produced and sold at a profit at a price of \$16 per month at volumes of 108,000 treatment courses per year.⁹

The global TB community has asked Janssen to drop the price of bedaquiline to a level no higher than \$32 per month—double the price at which researchers estimated bedaquiline could be sold for a profit. Doubling the price determined by researchers from the University of Liverpool is intended to account for current low volumes—only 25 percent of the 558,000 people estimated to have developed MDR-TB in 2017 were started on treatment,¹⁰ and most of these individuals did not receive bedaquiline. To date only 25,000 people have received bedaquiline worldwide.¹¹ In a open letter sent August 17, 2018, MSF urged Johnson & Johnson to recognize bedaquiline as “the fruit of a collective effort” and to lower its price to \$32 per month.¹² The TB community has asked the company to commit to further price reductions that are transparent, set in advance on the basis of pre-specified volume targets, and negotiated with global partners, including civil society.¹³

BEDAQUILINE AS A PUBLIC GOOD

The amount Janssen has invested in the research and development (R&D) of bedaquiline is not known due to a lack of transparency on the part of the company. Janssen has not made details of its expenditures on bedaquiline R&D public by, for example, publishing the costs of clinical trials or other R&D activities.

In addition to its own investments, the company has also benefited from substantial public investments in bedaquiline (see Tables 1 and 2). These publicly funded studies were necessary to inform the appropriate clinical use of bedaquiline, and some were even required to fulfill Janssen’s regulatory requirements. Janssen developed bedaquiline independently of other new drugs, and as an addition to a 24-month regimen of many other drugs with challenging side effects. Studies to inform how bedaquiline might optimize TB treatment by making it shorter or by replacing other toxic drugs in the regimen are ongoing. But the responsibility, and cost, for these studies has fallen largely on the public. Janssen has also cashed in on the variety of incentives the U.S. government offers to companies to develop treatments for orphan diseases such as TB.

TABLE 1. PUBLIC INVESTMENTS IN BEDAQUILINE'S DEVELOPMENT

STUDY NAME	DESCRIPTION	SPONSOR
ACTG A5343 NCT02583048	To evaluate the safety of bedaquiline when co-administered with novel TB drug, delamanid, for the treatment of MDR-TB.	NIAID
STREAM stage II NCT02409290	To evaluate whether bedaquiline can shorten treatment to six months or replace the injectable agent in the standardized 9–12-month regimen for the treatment of MDR-TB. *This study will serve as Janssen's phase III trial for bedaquiline, a condition of the accelerated approval granted by the FDA in 2012.	USAID
endTB NCT02754765	To evaluate six-month regimens composed of different combinations of bedaquiline, delamanid, linezolid, pyrazinamide, clofazimine, and moxifloxacin or levofloxacin for the treatment of MDR-TB.	Unitaid
NEXT NCT02454205	To evaluate 6–9 months of linezolid, bedaquiline, levofloxacin, pyrazinamide, and ethionamide/high dose isoniazid for the treatment of MDR-TB.	University of Cape Town
TB-PRACTECAL NCT02589782	To evaluate six-month regimens containing bedaquiline, pretomanid, and linezolid with and without moxifloxacin or clofazimine for the treatment of MDR-TB.	MSF
NC-003 NCT01691534	To evaluate the bactericidal activity of bedaquiline combined with pretomanid and pyrazinamide at two weeks. The results of NC-003 informed regimen selection for NC-005 (listed next).	TB Alliance *
NC-005 NCT02193776	To evaluate the early efficacy and safety of bedaquiline, pretomanid, and pyrazinamide, with and without moxifloxacin, over two months of treatment. The results of NC-005 informed regimen selection for SimpliciTB (listed next).	TB Alliance *
SimpliciTB NCT03338621	To evaluate four months of bedaquiline, pretomanid, moxifloxacin, and pyrazinamide for the treatment of DS-TB.	TB Alliance *
NIX-TB NCT02333799	To evaluate 6–9 months of bedaquiline, pretomanid, and linezolid for the treatment of XDR-TB and pre-XDR-TB.	TB Alliance *
ZeNix NCT03086486	To evaluate 6–9 months of bedaquiline and pretomanid when given with different doses and durations of linezolid for the treatment of XDR-TB, pre-XDR-TB, or treatment of intolerant or non-responsive MDR-TB.	TB Alliance *
TRUNCATE TB NCT03474198	To evaluate two-month regimens composed of first-line medicines in combination with new and repurposed second-line medicines for the treatment of DS-TB.	University College London
ACTG A5267 NCT00992069	To evaluate the safety and effect of bedaquiline when given with efavirenz to healthy volunteers.	NIAID
Janssen C211 NCT02354014	To determine the dose and safety of bedaquiline in children with MDR-TB, excluding those living with HIV. A Unitaid-funded pediatric TB project (the STEP-TB project) contributed \$1 million to this study, the conduct of which is a condition of the approval granted to Janssen by the EMA in 2014.	Unitaid
IMPAACT P1108 NCT02906007	To determine the dose and safety of bedaquiline in children with MDR-TB, including those living with HIV.	NIAID

NIAID: United States National Institutes of Allergy and Infectious Diseases

*The TB Alliance funds its trials with contributions from public and philanthropic donors.

TABLE 2. INCENTIVES FROM WHICH JANSSEN HAS BENEFITED

INCENTIVE	DESCRIPTION
U.S. Orphan Drug Tax Credit	<p>A USG tax credit worth up to 50% of annual R&D expenditures and other qualifying costs. This credit can be applied from the time of orphan drug designation up to approval. Bedaquiline was granted an orphan drug designation in January 2005 and approved by the FDA in December 2012.</p> <p>*Janssen also received a tax credit for the cost of its global donation program (60,000 six-month courses of bedaquiline).</p>
FDA marketing application fee exemption	<p>Sponsors of drugs awarded orphan drug designation are exempt from paying marketing application fees under the the U.S. Prescription Drug User Fee Act (PDUFA): \$1,841,500 in 2012.</p>
U.S. Tropical Disease Priority Review Voucher (PRV): PRV 204384	<p>Sponsors that successfully register a drug for a tropical disease with the FDA are awarded a PRV, which can be used to expedite FDA review of another product or sold to another sponsor. PRVs have sold for \$67–350 million.</p> <p>Janssen used its PRV to expedite FDA review of guselkumab (Tremfya), a blockbuster psoriasis drug that sells at nearly \$US 60,000 per patient per year in the U.S. and is estimated to yield US\$ 3.49 billion in sales by 2024. The PRV afforded Janssen a four-month jump on the market.</p>
Additional marketing exclusivity in the U.S. and Europe	<p>Sponsors that successfully register an orphan drug with the FDA are awarded seven years of marketing exclusivity from the time of approval in the U.S. (December 2012 through December 2019 in the case of bedaquiline).</p> <p>Sponsors that successfully register an orphan drug with the EMA are awarded ten years of marketing exclusivity from the time of approval in the European Union (March 2014 through March 2024 in the case of bedaquiline).</p>
<p>EMA: European Medicines Agency USG: United States Government</p>	

In addition to the public contributions underwriting bedaquiline’s development accounted for in Table 1, a substantial amount of public time and money has been invested in creating an enabling environment for the uptake of bedaquiline at the country level. The Unitaid-funded endTB project includes support for work to reduce barriers to bedaquiline access in 17 countries, expanding experience with and demand for the drug. Through Challenge TB, USAID has provided technical assistance to national TB programs in eight endTB project countries and an additional 15 countries. The technical assistance provided through endTB and Challenge TB has laid important foundations for, and in some instances directly facilitated, the introduction of bedaquiline in 20 of the 30 high MDR-TB burden countries. Treatment providers, including national TB programs, MSF, and other implementing partners have helped to document the safety, efficacy, and optimal use of bedaquiline for the treatment of MDR-TB. And civil society and community groups around the world have invested significant amounts of energy and resources in holding policy makers, regulatory authorities, donors, national TB programs, and other stakeholders accountable for improving access to bedaquiline.

MYTH VERSUS REALITY

A number of myths regarding bedaquiline pricing have circulated among members of the global TB community. Many of these myths have been perpetuated by claims Janssen has made, and are used to justify pricing bedaquiline out of the reach of TB programs and patients. We should not be fooled or distracted by these claims, and the section below dispels some of the more common, recalcitrant/pernicious myths.

✗ MYTH *“Price isn’t the problem, even with a global donation program we struggled to give the drug away for free.”*

✓ REALITY Many factors influence the adoption of new medicines. Affordability is not sufficient for ensuring access, but it is certainly necessary. TB programs may be slow to adopt new interventions for a variety of reasons, including a lack of awareness of drug availability and procurement processes; limited availability of technical expertise; confusion regarding WHO requirements and conditions for introduction; limited availability of data from clinical trials; challenges updating national guidelines; difficulties in import and customs clearance; limited access to companion technologies; and a lack of high-level national government support.¹⁴ We anticipate that, with greatly increased familiarity and experience with bedaquiline, strong WHO guidance for its use, and countries such as South Africa having already switched to bedaquiline-based regimens, demand will rapidly increase, so long as price is not a barrier.

✗ MYTH *“Janssen invested \$500M in developing bedaquiline and needs to recoup these investments in order to continue to invest in R&D.”*

✓ REALITY We would welcome a transparent, detailed, and verifiable account of Janssen’s investments in bedaquiline, which to date has not been made available. In addition to its direct expenditures, Janssen benefited from public research and other investments and took advantage of several incentives designed to stimulate investments in R&D for diseases in which a return on investment is unlikely or unrealistic. Janssen has likely recouped the value of any claimed investment costs through the public support, incentives, and tax credits listed in Tables 1 and 2. There is also the additional, unquantifiable value of public relations and good press Janssen has received for developing a drug for a neglected disease.

✗ MYTH *“Janssen also invested in supporting TB health systems strengthening and national TB programs to set up pharmacovigilance systems.”*

✓ REALITY Janssen has pointed to its support for TB programs—which also has not been transparently enumerated—as further reason why they need to recoup costs through drug sales and thus high pricing. Although these infusions may have been useful to programs, they are likely small (especially for a multibillion dollar company), they have provided Janssen with opportunities to further its public image and relations, and were made under the guise of support rather than named as costs that would need to be recouped in the price Janssen sets for the drug.

X MYTH *“The high price of bedaquiline is justified and reasonable given the anticipated savings that will be passed on to health systems”*

✓ REALITY Because bedaquiline is more effective than many other TB drugs, using it may result in savings in the long run. But any savings incurred by the health system from using superior products should be reinvested in strengthening the TB response, not boosting pharmaceutical company profits. Currently, 75 percent of people with RR-/MDR-TB are never diagnosed or started on appropriate treatment, and there is a \$3.5 billion gap in funding for TB programs worldwide.¹⁵ TB programs need all the savings they can get—not so pharma can profit—but so TB programs can do much more with their limited budgets. A recent report by Oxfam shows how Johnson & Johnson and other pharmaceutical companies have used tax avoidance schemes to deprive governments of billions of dollars in tax revenues. When companies avoid paying their fair share of taxes, governments often must increase consumption taxes to make up for the shortfall of corporate tax dollars. “Patients thus often pay twice for medicines: through their tax dollars and at the pharmacy—or three times if we count the extra tax dollars we pay because companies don’t.”¹⁶ Johnson & Johnson and the pharmaceutical industry at large are starving the same governments of the resources on which their profits depend, including the support of publicly funded research, public drug certification, public procurement, and public protection of intellectual property.¹⁷ Health systems would be better served by public coffers that are not starved for resources by pharmaceutical industry tax avoidance.

CONCLUSION

The public has made significant investments in the development and introduction of bedaquiline. In many instances, public funding has supported critical work left unfinished by Janssen. As such, credit for bedaquiline’s development belongs in large part to the public. The price of bedaquiline should reflect the public’s investment and, to quote Johnson & Johnson’s corporate credo, put the needs and well-being of the people it serves first.

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