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Public Investments in the Clinical Development of Bedaquiline

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Treatment Action Group

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For TAG's full policy on managing potential conflicts of interest:

http://www.treatmentactiongroup.org/content/tags-policy-managing-conflicts-interest.

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Background

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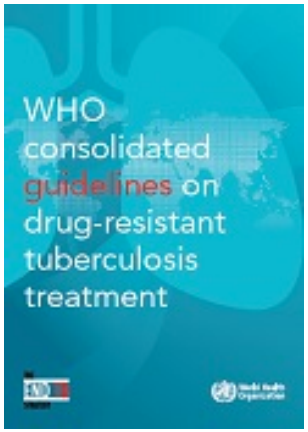
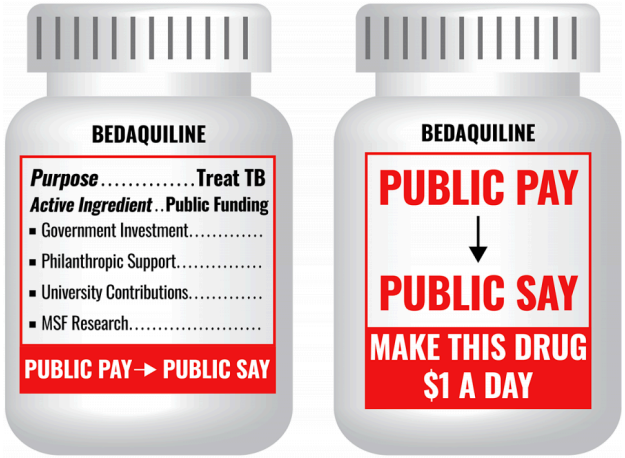
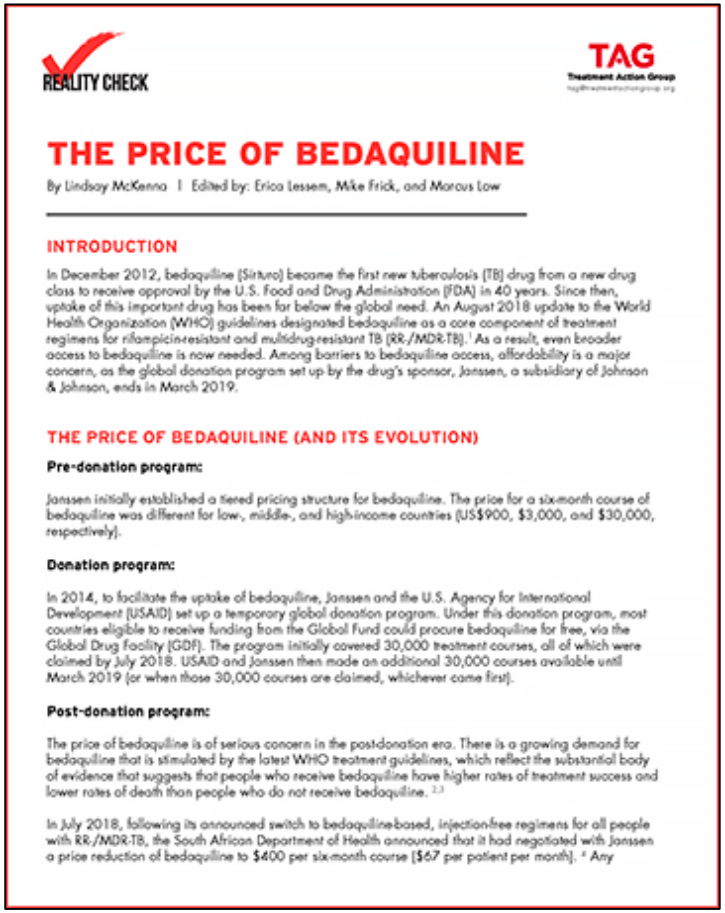
- 2018/19 WHO RR-/MDR-TB Guidelines
- 2019 J&J/USAID global donation program end
- $400 per 188 tablets available via GDF
- D. Gotham et al → $1/day campaign
- Public pay, public say; bedaquiline as a public good







REALITY CHECK

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THE PRICE OF BEDAQUILINE

By Lindsay McKenna | Edited by: Erica Lessem, Mike Frick, and Marcus Low

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).

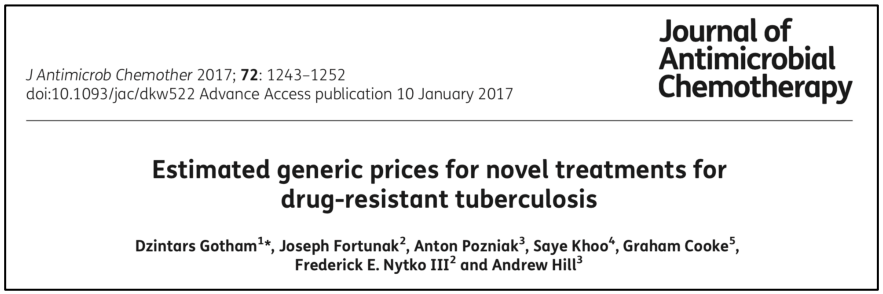
Donation program:

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



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Journal of Antimicrobial Chemotherapy

Estimated generic prices for novel treatments for drug-resistant tuberculosis

Dzintars Gotham[1]*, Joseph Fortunak[2], Anton Pozniak[3], Saye Khoo[4], Graham Cooke[5], Frederick E. Nytko III[2] and Andrew Hill[3]

- http://www.treatmentactiongroup.org/content/reality-check-price-of-bedaquiline
- https://doi.org/10.1093/jac/dkw522
- https://www.msfaccess.org/msf-launches-global-campaign-urging-johnson-johnson-reduce-price-life-saving-tb-drug
- http://www.stoptb.org/gdf/drugsupply/bedaquiline.asp

Methods: quantifying public & philanthropic investments

- Identified various avenues of public investments in BDQ's development: clinical trials, donation program; tax credits + deductions; priority review voucher (PRV) revenues.
- Gathered data on investments through contact with study leads/ funders.
- Substituted + adjusted published average costs for non-responses (Sertkaya, 2016).
- Calculated tax credits + deductions based on estimated originator trial costs + donation expenses.
- Applied a published model to estimate PRV value (Ridley, 2016).

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How did we substitute and adjust published average costs (for non-responses)?

- We generated a range of clinical trial cost estimates by using Sertkaya, 2016 estimates as the maximum of the range:
  - Phase I: US$ 4.9 million
  - Phase II: US$ 16.5 million
  - Phase III: US$ 26.6 million
- For lower-bound, we accounted for lower clinical trial costs in LMICs and proportion of multidrug trial costs attributable to BDQ development:
  - Assumed studies in LMICs cost 40% lower compared to US (Frost, 2016);
  - Determined how many “investigational foci” or “key research questions” in each study and assigned percentage accordingly.

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How did we calculate proportion of costs attributable to bedaquiline?

Study Name	% Attributed to BDQ	Rationale
NEXT	100%	BDQ is the key investigational drug in this study
endTB observational	50%	BDQ and DLM are both primary investigational medicines in this study
endTB interventional	50%	BDQ and DLM are both primary investigational medicines in this study
endTB-Q	50%	BDQ and DLM are both primary investigational medicines in this study
ACTG 5343	50%	BDQ and DLM are both primary investigational medicines in this study
STREAM	50%	The study has two key areas of focus: the use of a shortened regimen without BDQ, and the use of shortened regimens including BDQ. BDQ is included in two of the three experimental arms in this study.

Determined how many “investigational foci” or “key research questions” in each study and assigned percentage accordingly.

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Tax credits, deductions, and the PRV

Orphan drug tax credits

- 50% of qualifying research expenditures, 2005–2012; estimated average clinical trial cost by phase to estimate total research expenditures = $43–72M → $22–36M tax credits

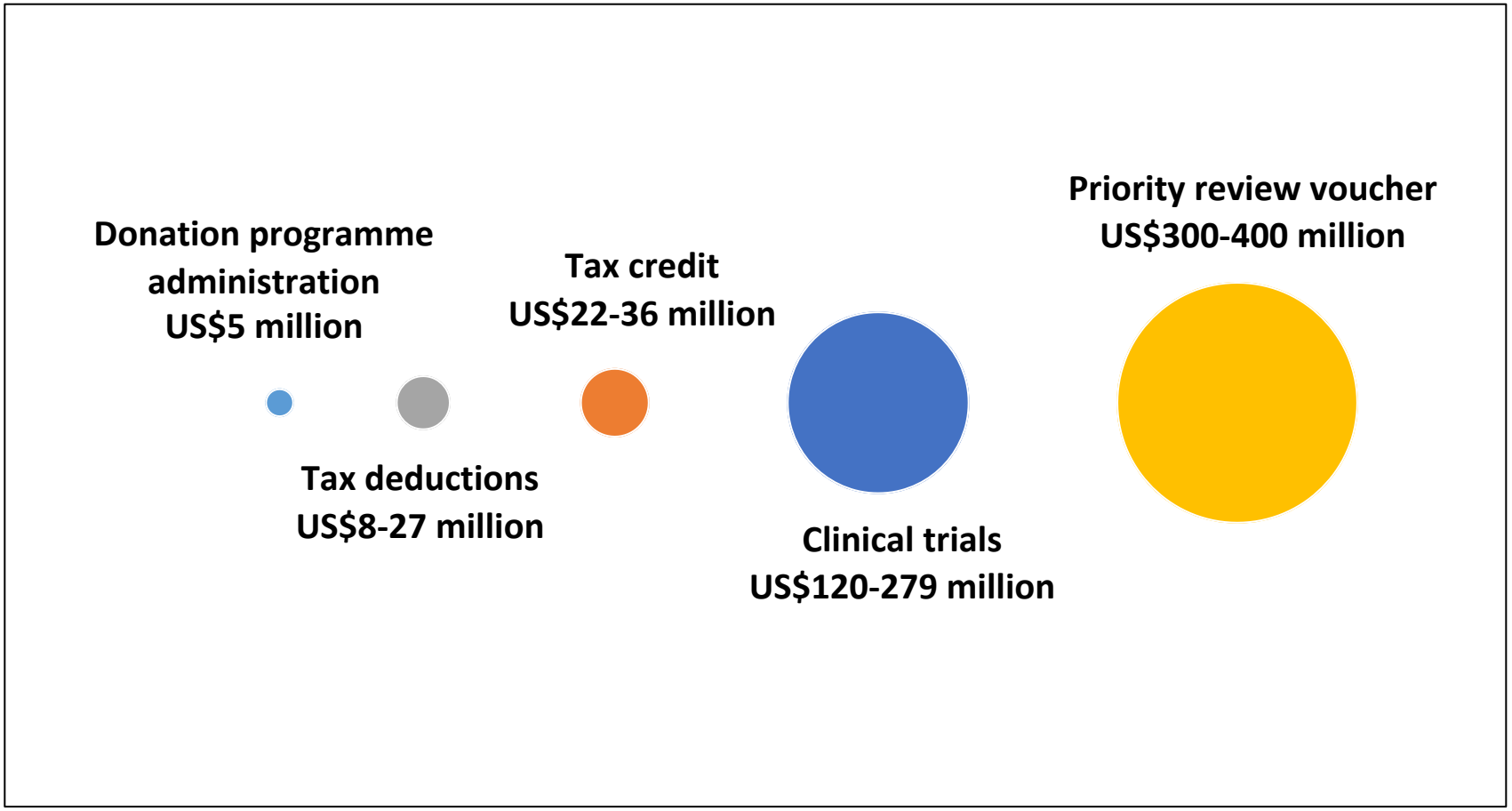
Tax deductions applied to global donation program, 2015–2019

1. based on cost of manufacture for bedaquiline, as reported by a Janssen representative (deductible expense is twice the cost of making the product – aka cost basis – or the midpoint between cost basis and fair market value, whichever is lower); $266 per course x 105,000 treatment courses = the deductible expense claimed after inflation adjustment: 28.3M → $8.4M reduction in tax bill;
2. based on reports on charitable contributions published by Janssen; deductible expense claimed after inflation adjustment for 2015–2016: $76.5M → $26.7M reduction in tax bill

Priority Review Voucher (PRV) – used by Janssen to expedite FDA review of NDA for guselkumab (for plaque psoriasis)

- Ridley 2016 model estimates PRV value based on (1) acceleration of approval in months [4 months]; and (2) fifth-year [2022] sales of product to which PRV is applied [US$1.6B].

Results: Public Sector Investments in the Development of Bedaquiline



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Results: Overall Estimated Public vs. Originator Investments in Bedaquiline

(2018 US$ millions)

	Public	Originator	Ratio of public to originator expenditures*
Clinical trials			
Out of pocket	120-279	76-163	1·6-1·7
Capitalized	142-328	115-280	0·9-1·2
Capitalized and risk-adjusted	312-733	278-695	1·05-1·12
Funding through PRV	300-400	-	-
Orphan drug tax credit	22-36	-	-
Bedaquiline donation program	13-32†	14-77	0·4-0·9
Totals			
Out-of-pocket expenditures	455-747	90-240	3·1-5·0
Capitalized and risk-adjusted expenditures	647-1,201	292-772	1·6-2·2

*Ranges for ratios are calculated as the bottom of the range for public funding divided by bottom of the range for Janssen funding, and top of the range for public funding divided by top of the range for originator funding.

†Composed of US$8-27 million through tax deductions for originator and US$5 million through public funding of administration of the donation programme.

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Conclusions

- We estimate that total public expenditures have been 3·1–5·0 times those of the originator (US$455-747 million versus US$90-240 million), or 1·6–2·2 (US$647-1,201 million versus US$292-772 million) when the cost of failures and costs of forgoing other investment opportunities are counted.
- Quantifying these investments can contribute to debates concerning the price of bedaquiline, the role of the public sector in pharmaceutical research and development (R&D), and the costs of bringing a novel medicine to market.
- Our analysis provides a methodology that may be adapted to estimate public investments in the development of other TB medicines, such as pretomanid and rifapentine.

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Limitations

- Pre-clinical investments were not assessed.
- Our estimates rely on estimated overall trial costs reported by study sponsors or lead investigators.
- Our estimates also rely, in part, on average clinical trial costs reported by a US-based industry analysis group (Sertkaya, 2016).
- Estimated average costs were phase-specific and adjusted for potentially lower trial costs in LMICs and proportion attributable to bedaquiline, but costs were not adjusted to take into account different trial characteristics such as enrolment numbers or duration of treatment and/or follow up.
- Public investments in technical assistance work and cohort studies were not captured.

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Acknowledgements

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