Policy Brief #03: August 2021

GLOBAL AMR R&D HUB

Informing Policy Action to Secure New Antibiotics

Based on the study

Estimating global patient needs and market potential for priority health technologies addressing antimicrobial resistance

Priority Needs for New Antibiotics

A steady supply of new antibiotics is a growing imperative. As the rate of development of new agents slows and resistance grows, the 'replenishment factor' continues to wane – with implications for modern medicine[1] beyond our ability to treat bacterial infections. The patent-based system links the development of new antibiotics to their commercialization in one chain, where the developer reaps the 'return' on its' earlier development 'investment' (and risk) with a time-delay of over a decade. Currently, low investment returns from sales are considered a key reason for the low quantity and quality of pipeline innovation[2]. A recently published Global AMR R&D Hub study (see Info Box below) aimed to explore this further[3]. The needed new antibiotics (such as those defined for this study - see **'EAG's Prioritised Antibiotics'**) are considered unlikely to reach the market in 2025. Additionally, to reach the priority high-need patient groups, further development, studies and resources will be required following initial licensure.

Modelling AMR Markets & Needs

A multidisciplinary, global, Expert Advisory Group (EAG) was formed to identify – initially through a human patient-need approach – some of the highest AMR patient needs for new health technologies. The four profiles (2 x diagnostics [Dx]; 2 x antibiotics [Tx]) were then quantified in terms of the need (patient numbers) & market potential (peak revenues) to generate global (80% of the world) forecasts to 2040[3].

Quantifying the patient need used a static bottom-up epidemiological model; the market potential a top-down model using the existing market for branded Gram negative antibiotics as its basis. Uncertainty of the commercial estimates and market lever possibilities were explored through 'What If' scenarios.

EAG'S PRIORITISED ANTIBIOTICS

2x small-molecule antibiotics with activity against MDR bacteria for the treatment of:

- **Tx1 (BSI) = Blood stream infections**
- **Tx2 (PNU) = Pneumonia infections**

- Intravenous (IV) administration to treat severely ill hospitalised patients[4]
- Currently all 'critical priorities' are Gram negative bacteria and would be considered RESERVE antibiotics for stewardship purposes[5]

Meeting Priority Needs will Result in Weak Rewards

Revenue is determined by the amount and price that buyers in the market (national healthcare payors) are able, or willing, to pay. The priority antibiotics were forecast to generate **$184m** for Tx1 (BSI) and **$127m** for Tx2 (PNU) in sales revenue by securing a **7.4%** and **5.3% patient share,** respectively, at their market peak in 2036 (comparing unfavourably with conservatively estimated pre-launch development costs of between $200-$300m). This assumes the product would be launched in the USA (in 2025) into a branded, intravenous (IV) Gram negative market currently worth ~$500m in sales from 70+ countries worldwide.

The investment case appears weakest where the unmet needs are the highest

Current pre-licensure ('push') public/philanthropic support for product development of such high public health importance needs to be flanked by strong action on the post-licensure ('pull') side of the market. This is to ensure that not only these products reach the market but that these investments are also able to yield the full breadth of their patient and societal benefits.

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[1] The Global Response to AMR Momentum, success, and critical gaps. Wellcome Trust; 2020.
[2] 2020 Antibacterial agents in clinical and preclinical development: an overview and analysis. Geneva: World Health Organization; 2021.
[3] Estimating global patient needs and market potential for priority health technologies addressing antimicrobial resistance; 2021: https://bit.ly/3CUpDKk
[4] Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics, World Health Organisation; 2017.
[5] The 2019 WHO AWaRe classification of antibiotics for evaluation and monitoring of use. Geneva: World Health Organization; 2019. (WHO/EMP/IAU/2019.11).]

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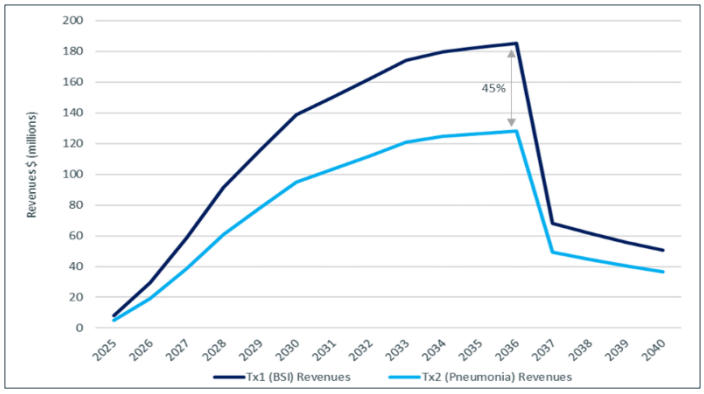

Figure A. *Projected global revenues 2020-2040 for Tx1 & Tx2.*

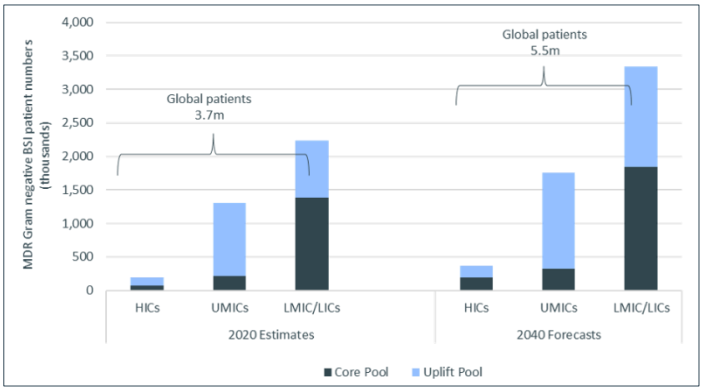

Figure B. *Projected patient needs for Tx1 (BSI) by income-group. Estimate derived from core pool of 13 countries; uplift pool - extrapolation from 8 more.*

Global Patient Burden & Need is Growing Everywhere

Figure A shows that revenues are expected to be higher from Tx1 (BSI) than Tx2 (PNU) [6], despite all-cause pneumonia currently having a 1.5 times higher global disease burden than BSI. This is due to the higher Gram negative bacterial prevalence in BSI and the different pathogen proportions. **BSI has the larger burden of multidrug resistant (MDR) Gram negative cases than pneumonia by almost twice** and therefore the higher need for new alternative antibiotics.

By 2040, 8.3 million people in 80% of the world will face MDR BSI or PNU [7] & a high need for new treatment options

Of the six critical Gram negative pathogens prevalent in the two syndromes, five are common across the two. There were an estimated 3.7 million cases of MDR BSI and 1.7 million cases of MDR pneumonia attributable to Gram negative pathogens worldwide in 2020. Patient numbers are forecast **to rise to 5.5 million cases of MDR BSI and 2.8 million cases of MDR pneumonia by 2040**.

Blood Stream Infections

Represent a proxy for the some of the most critical needs - when an infection begins to overwhelm the body, moving from a single tissue site to a critical systemic infection. Despite a high MDR/extensively drug resistant burden, it is not an antibiotic indication.

Market Access Model; Diminishing Ability to Meet Need

Figure B shows how the disproportionate increase in the forecasted burden will fall in lower-middle and low-income countries (LMICs/LICs) – a finding across both need profiles. Bringing this patient need together with the commercial modelling shows that the patients forecast to actually receive one of the modelled antibiotics in 2035 (i.e., the year before patent expiry) equates to **less than 1% of a forecasted 7 million accessible patients**[8] outside high-income countries (HICs).

The weak investment case also negatively impacts the products' ability to reach the countries & patient groups facing the highest need

Our forecasts indicate a worsening access gap whereby efficacious antibiotics are not available in the parts of the world at the scale where the need is dominant and growing most rapidly. With need spread thinly across many national markets access will likely be particularly precarious, also in some HICs.

Neonatal Sepsis

Tx1 (BSI) could be a new treatment for neonatal sepsis but could only be achieved subsequently and sequentially (adult – adolescent – child – infants) following initial licensure and requiring substantial further resources.

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[6] The modelling assumed these represent two distinct, non-cannibalizing products, which may not be the case

[7] For only these two syndromes & critical causative pathogens

[8] Includes only those with existing access to branded antibiotics

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Market Intervention Necessary – At What Scale?

Further public/philanthropic support for these markets is warranted given the public health importance and the weak investment case, which are compounded by multiple other challenges around data generation and licensing in the countries and patient groups facing the highest need.

Delinking Rewards from Volumes

Extensive literature elsewhere has highlighted the importance of delinked solutions in this field. While beyond the scope of this study, USA, UK & Sweden are in various stages of proposing, testing and implementing such measures.

Scenarios explored in this study indicate both the necessity for – and the limitations of – policy levers available under the current market system (i.e., price, volume and patents) to sufficiently improve market potentials.

Health system policy innovation – & collaborative action – is required now to secure tomorrow's innovation

The specific features of these markets (the stewardship imperative, slow uptake, low and fragmented global volumes and cheap and plentiful[9] older antibiotics) suggest that additional **support and/or implementation of new models will be required** in addition to the use of traditional policy levers[10].

VOLUME-BASED MARKET SCENARIO'S

A possible Gram negative antibiotic market (volume) contracting scenario – of around 30%[11] – is forecast to reduce peak revenues to around $50 million per antibiotic; this market-eliminating scenario is currently considered more likely than one that enables the 4-fold increase in market-share-capture (by an individual antibiotic), forecast to restore market attractiveness.

PRICING-BASED MARKET SCENARIOS

Were only 10 high-income G20 countries able to increase their valuations/willingness to pay for such needed new products, prices would need to increase by around 5-fold to reach even the lower 'attractiveness threshold' of $400m in peak sales. Were all 70+ currently purchasing countries able to do so, then a tripling or quadrupling of current prices would be necessary to reach this level threshold[12].

In light of the findings of the therapeutic workstream of this study, the EAG made the **following recommendations**:

- Widespread and immediate use of existing policy levers (i.e., national-level reform of pricing and reimbursement – ideally backed by broader value-assessment frameworks) is required.
- National efforts should be coupled with additional pull support measures – perhaps at the market segment level – to reach a scale of return on investment attractive for developers.
- Substantially progress the dialogue on possible global access and distribution mechanisms taking into account the need for both access and stewardship.
- Further exploration of the following:
  - Options to stabilise the priority antibiotic market segment beyond individual products.
  - Feasibility of implementing delinkage across more countries.
  - If and how voluntary cooperation for demand-aggregation could occur.
  - Mobilisation of donor-support / coordination options for LMICs/LICs.

With many thanks to all those who generously gave their time & insights to this study

The study is available for download from: https://globalamrhub.org/our-work/studies/market-potential-and-priority-patient-needs/

For questions or enquiries please contact: Global AMR R&D Hub

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[9] if increasingly redundant

[10] was explored further in Policy Brief No.2 [https://globalamrhub.org/our-work/studies/market-potential-and-priority-patient-needs/]

[11] From 2019 patient numbers

[12] This simplified analysis does not consider price-volume relationship