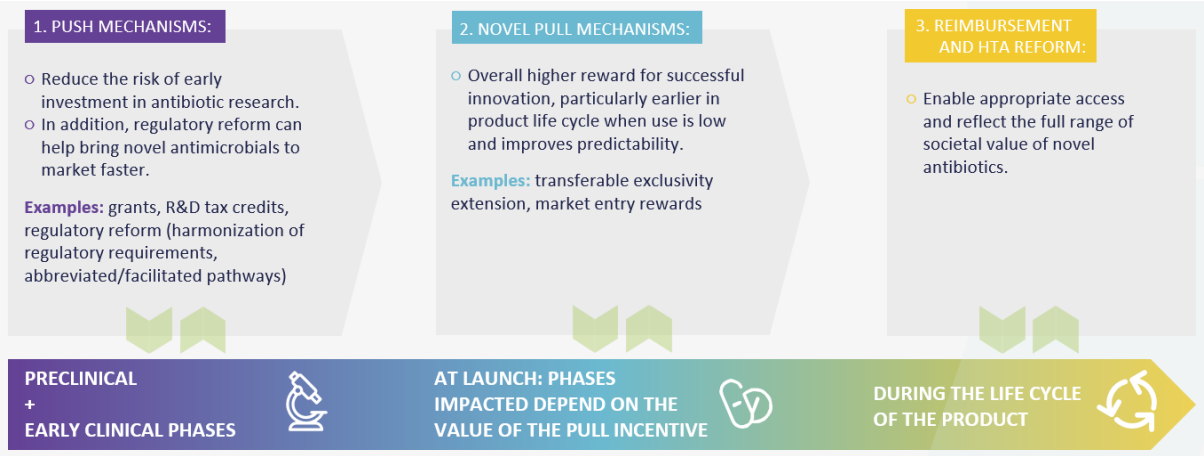
Policy Position

Reimbursement and Health Technology Assessment Reform

Antimicrobial resistance (AMR) is a significant threat to global health security and undermines the achievements of modern medicine. New antibiotics, vaccines, and other innovations are urgently needed; however, there are relatively few in development. Over the past two decades, there has been a significant decline in the number of companies conducting antibiotic and antifungal R&D due to the significant scientific, regulatory, and economic challenges specific to this therapeutic area[i].

If governments can support market conditions where there is a predictable and sustainable return on investment, the pharmaceutical industry and private investors have demonstrated their willingness to take on the necessary risk and uncertainty that comes with the development of an approved medicine. Adoption of the following suite of incentives by governments would address challenges across the antibiotic product life cycle and meaningfully impact investment decisions.

Figure 1: Suite of incentives



Reimbursement and HTA reform
There are opportunities to incentivize antibiotic innovation and stabilize the economics of antibiotic R&D through existing systems.

Reimbursement reform for hospital-administered antibiotics would enable appropriate access to novel antibiotics by removing barriers posed by bundled-payment mechanisms. Reimbursement reform can complement and reinforce key antimicrobial stewardship components, including the use of diagnostics, de-escalation, regimen monitoring, and surveillance. These can support appropriate use to preserve existing treatments / alternative treatment options. Reimbursement reform should also result in predictability in costs for the health system and reflect the value of a novel antibiotic over its life-cycle.
Payer reform is needed to better capture the societal value of antibiotics in Health Technology Assessments (HTA). The objective is to create an evidence-based value assessment that then can serve as a foundation for commercial discussions.

These reforms can be undertaken in the short-term within existing systems to improve appropriate patient access and strengthen market the economics of antibiotic R&D. They form an important part of the suite of incentives needed to sustainably stimulate antimicrobial R&D.

Current HTA and reimbursement practices for antibiotics

According to the World Health Organization, "Health Technology Assessment" (HTA) is the systematic evaluation of properties, effects and/or impacts of health technologies and interventions. It covers both the direct, intended consequences of technologies and interventions as well as their indirect, unintended consequences. The approach informs policy and decision-making in health care, especially on how best to allocate limited funds to health interventions and technologies[ii].

Conducting HTA for antibiotics is challenging because of the multiple "indirect" benefits associated with antibiotic use. A new and effective antibiotic treatment might initially have its clinical use limited. Therefore, at least part of the value of the new antibiotic is based upon its "insurance value" to the patient and to the clinical community. That is, its value comes not from its use but rather from the benefit of having an effective treatment available in case of resistant infections (e.g. outbreaks, increases in prevalence) and enabling other procedures reliant on antibiotics (e.g. chemotherapy, surgeries).

Current HTA processes do not assess the unique attributes of novel antibiotics or consider the full range of benefits these important technologies bring to patients, healthcare systems and society in reimbursement decision making[iii]. While effective new antibiotics provide a range of benefits to society, there is still a low value placed on them. This is largely due to the availability of generic antibiotics that are effective (and appropriate) in treating patients with susceptible infections and the fact that novel antibiotics are often approved based on non-inferiority clinical trials and small patient sets, which were put in place by regulatory agencies to facilitate antibiotic development. It is not possible or feasible to require superiority trials for novel antibiotics, given ethical concerns and operational challenges. Further data on the benefits novel antibiotics provide by targeting resistant pathogens, for example, should be considered by reimbursement agencies. This calls for a broader consideration of value beyond traditional reimbursement approaches to ensure patients have access to important new antibiotics and reimbursement provides a sufficient return on investment to incentivize further research and development. The issue of reimbursement was acknowledged by the European Union in its AMR Action Plan that was launched in June 2017, which commits to "develop new or improved methodological HTA approaches and foster methodological consensus-building."

Appropriate use of antibiotics can be directly impacted by reimbursement mechanisms as it defines the range of therapeutic options (both new and old antibiotics) available to treat infections. The current Diagnosis-Related Group-based (DRG) hospital reimbursement system used in the U.S., most of Europe and Japan imposes a strict budget constraint to treat patients in hospital settings which can impede or delay the prescription of higher priced novel antibiotics – even when they are the most appropriate treatment. Reimbursing certain antibiotics outside bundled payments for inpatient stays would facilitate better stewardship, especially if coupled with mechanisms to ensure appropriate use.

Assess the full value of antibiotics

The Office of Health Economics[iv] and DRIVE AB[v] released reports in 2017 and 2018 respectively, presenting the reasons why considering additional elements to assess the value of antibiotics are

needed. Both reports highlight elements that more accurately reflect the full range of benefits provided by antibiotics that are not typically included in current HTA methods:

- **Transmission value** includes all benefits of avoiding the spread of infection to the wider population.
- **Insurance value** refers to the value of having a treatment available in case of a future major or rapidly escalating health problem.
- **Diversity value** refers to the benefits of reducing "selection pressure" (i.e. when an antibiotic fails to eradicate resistant strains, which then survive and multiply to create a resistance problem) and thus preserving the efficacy of existing antibiotics.
- **Novel action value** refers to the potential value associated with an antibiotic having a new or unique mechanism of action (MOA) or representing a new chemical structure i.e. first in class, which will provide "spillover" benefits.
- **Enablement value** is the value associated with enabling other treatments or procedures, e.g. surgery and chemotherapy.
- **Spectrum value** refers to the value associated with narrow spectrum antibiotics, which may be more valuable than broad spectrum antibiotics because they could reduce the spread of AMR by preventing 'collateral damage' to the microbiome.

Why do we need reimbursement and HTA reform urgently?

The current HTA practice, which does not fully consider the value novel antibiotics bring to society, acts as a disincentive for investments in R&D. Research has shown that the current reimbursement environment negatively impacts investment by antibiotics developers because the return on new antibiotics is far less than the societal value that these drugs deliver[vi]. In its final recommendations, DRIVE AB asks national authorities to develop HTA processes that better capture the societal value of antibiotics in coverage and reimbursement decision-making as an important tool to maintain current private investment into antibiotic R&D[v]. Currently HTA and reimbursement criteria are not based on the value antibiotics bring to patients and society as a whole.

What is being done to address these challenges?

Policymakers have recognized the role that HTA and reimbursement systems can play to incentivize investment in antimicrobial R&D and enable appropriate patient access. Several proposals have been made in the United States[vii], the United Kingdom,[viii,ix] Germany[x], France and Japan[xi] but to date none have been implemented.

Recommendation and call to action

As discussions on pull incentives progress, national authorities should address the economic challenges within their existing systems. This will ensure that incentives for antibiotic innovation can be improved in the near term to maintain current private investment into antibiotic R&D. Urgent action is needed to develop and implement HTA processes to better capture the societal value of antibiotics in coverage and reimbursement decision-making and enable access to life saving medicines. Reimbursement reform for hospital-administered antibiotics would remove barriers to access posed by bundled-payment mechanisms that discourage appropriate use of novel antibiotics.

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