Transferable exclusivity voucher: a flawed incentive to stimulate antibiotic innovation

As antibiotic resistance increases globally, antibiotic innovation is struggling. WHO states that the antibiotic clinical pipeline is "insufficient to tackle the challenge of increasing emergence and spread of antimicrobial resistance".[1] To prevent the development of resistance, new antibiotics are used as last resort treatments and, if properly used, have small patient populations, resulting in fairly low sales revenues for industry.

Several incentives have been proposed to stimulate antibiotic innovation.[2–4] The pharmaceutical industry champions the transferable exclusivity voucher for European implementation.[5,6] The voucher is a complex, untested incentive. In theory, a developer would be awarded a voucher with the regulatory approval of an important new antibiotic. This voucher could then be applied to one non-related medicine (eg, a cancer immunotherapy), extending its patent period up to 1 year. If the antibiotic developer does not want to use the voucher, the company could sell it. This indirect transaction is expected to generate a lucrative one-time payment for the antibiotic innovator.[5]

The European Commission (EC) is expected to include the voucher in its proposed revision of the pharmaceutical legislation, expected in March, 2023.[7] This decision would be unfortunate since there are fundamental problems with the transferable exclusivity voucher.

The voucher decouples payment from accessibility so that countries would be forced to pay indirectly for the new antibiotic through extended monopoly prices of a blockbuster medicine (ie, those exceeding €1 billion in annual revenues) with no guarantee of access to the antibiotic. Regulatory approval is only the first step to medicine availability and is often followed by health technology assessment and price negotiations. New medicines typically take years to become available in European countries after EC approval. For example, only three European countries had access to meropenem–vaborbactam, an antibiotic included in WHO's Essential Medicines List as a reserve antibiotic, 2 years after EC approval.[8] A transferable exclusivity voucher forces countries to pay for an antibiotic that is unavailable to patients. Importantly, the voucher will not promote equitable global access to new antibiotics, contrary to an aim of the 2022 EU Global Health Strategy of "enhanced equity in the access to vaccines and other [medical] countermeasures".[9]

The transferable exclusivity voucher will probably be unpredictably expensive. The cost to European countries is estimated at €350–840 million per voucher (the difference between the monopoly and generic or biosimilar prices).[5,6] These estimates are likely to underestimate the true costs to payers because the data are from industry-sponsored reports in which the authors average annual sales of biopharmaceuticals in their final exclusivity year, including those with moderate sales.[5] Yet the voucher would only be applied to the most profitable medicines, so averaging reduces the estimated cost of the voucher substantially. It is difficult to give precise voucher cost estimates since pharmaceutical sales revenues are not publicly available, but a top grossing European medicine might reap €5 billion or more in annual peak sales—an amount five to ten times more costly than Europe's proposed share of other scientifically analysed incentives necessary to stimulate antibiotic innovation.[10–12]

The pharmaceutical industry estimates that up to three vouchers could be awarded every year.[5,6] This is unrealistic. There are few antibiotics in clinical development that are likely to meet European public health needs.[1] Unfortunately, at this time, anticipating awards for even one antibiotic per year implies rewarding antibiotics of questionable public health value and little global value. If eligibility requirements for a transferable exclusivity voucher would be implemented more stringently, allowing perhaps only one or two antibiotics to qualify in the next 10 years, this would be expected to reduce the motivation of innovators—the opposite of the intended effect.

Even with a stronger antibiotic pipeline, there is little public health need for three new antibiotics every year. These scarce public health funds should be balanced with infection prevention and control and antibiotic stewardship measures. From a purely economic perspective, it is more cost-effective to invest in interventions that would reduce all multidrug-resistant pathogens rather than in multiple antibiotics impacting only a few pathogens or resistance patterns.[3,13]

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As European countries struggle to make novel, effective, high-priced medicines accessible, the transferable exclusivity voucher will prolong inaccessibility and could disproportionately affect patients with rare diseases.[14] Novel medicines that treat only 2–3% of patients are anticipated to constitute half of high-income country pharmaceutical expenditure by 2026.[15] Additionally, a transferable exclusivity voucher could have detrimental effects on the development of biosimilars. Given the time-consuming and expensive development pathways, an unexpected 1-year delay could increase the unit prices of biosimilars to account for the costs of downtime.

If the EC had attempted and failed to implement other recommended incentives to stimulate antibiotic innovation, it would be justified to move forward with a transferable exclusivity voucher as a last-ditch effort. Yet no such action has taken place. Indeed, by putting forward the voucher the EC is undercutting the actions of its own Health Emergency Preparedness and Response Authority (HERA), which has commissioned further analyses of incentives for antibiotic access and innovation including a European-wide annual revenue guarantee.[16–18] This incentive aims to simultaneously stimulate innovation and secure access to important antibiotics by paying guaranteed amounts for access to selected antibiotics, rather than consumption. This approach is currently being piloted in different versions in England and Sweden.[19,20]

Legislating an untested voucher with these deficiencies into the new updated European pharmaceutical legislation is not advisable. Many European member states do not support the voucher for many of the reasons we have discussed.[7] Antibiotic innovators need attractive financial returns, but in fair and predictable ways, in collaboration with European countries and their public health priorities.

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