Transferable exclusivity extensions to stimulate antibiotic research and development: what is at stake?

Published Online December 2, 2022 https://doi.org/10.1016/S2666-5247(22)00336-6

Getting new and innovative antibiotics to market is important to tackle growing antibiotic resistance.[1] However, the pharmaceutical industry has been reluctant to invest in antibiotic research and development because of small sales volumes and low prices, resulting in poor returns on investment. For the 18 new antibiotics approved since 2010, the median annual sales in the first year following launch was USD $16 million;[2] four antibiotic developers have filed for bankruptcy since April, 2019.[3] It is often so financially risky to launch a new antibiotic that launches are restricted to commercially viable markets, such as the USA, the UK, and Sweden.[2] To encourage antibiotic research and development, the European Commission is considering use of transferable exclusivity extension (TEE) vouchers.[4]

TEE vouchers would be granted to antibiotic developers that successfully develop and launch new antibiotics. The developer can use the voucher to extend the patent term of any medication in EU countries by up to 12 months or sell the voucher to another pharmaceutical company. Companies are likely to apply TEEs to expensive, high-selling, brand-name medicines to maximise revenues. The pharmaceutical industry has been supportive of TEEs, arguing that they do not require upfront government funding, provide a large financial incentive, and would benefit pharmaceutical companies of all sizes.[5] However, there are important concerns to consider before implementing TEEs.

First, TEEs would be associated with substantial financial costs to national health-care systems across Europe. The exact effects of TEEs are difficult to establish, since any estimate is sensitive to the number of TEEs granted and the impact of generic market entry on prices. Independent researchers estimated that the cost to European health-care systems for a 12-month TEE could exceed €3 billion,[6] whereas an industry-sponsored analysis placed the cost of each TEE at less than €1 billion.[7] There are also concerns that TEEs would delay the improved access to medicines that often follows generic market entry.[4,8]

Second, it is unclear to what extent TEEs would incentivise antibiotic research and development. Evaluations of other market entry rewards, such as advanced market commitments for pneumococcal conjugate vaccines[9] and priority review vouchers for therapeutic areas with unmet need,[10] found that they had a minimal effect on research and development. Instead, they brought forward supply of medications already in the late stages of development. However, the effect of any incentive is likely to be dependent on the size of the reward, and it is undeniable that TEEs would provide a large incentive to the pharmaceutical industry.

Third, TEEs do not ensure access to new antibiotics. As TEEs are a one-off reward, there is a risk that antibiotic developers could choose to only launch new antibiotics in member states where they expect reasonable profits. Even if TEEs include strict access conditions, there is no guarantee that antibiotic developers will not later file for bankruptcy. Many commentators have argued the only sustainable way to create a viable market for antibiotics is through regular payments that delink volume of sales and reimbursement.[2,3,11] This solution also ensures that antibiotic developers remain financially sustainable. This is the rationale behind the subscription-style payments for new antibiotics that have been applied in the UK and Sweden.[11]

Fourth, TEEs do not necessarily link the clinical value of new antibiotics to the size of reward. This is because the value of a TEE is determined by which expensive, high-selling, brand-name medicines are nearing patent expiry when it is granted. It would be more efficient to reward developers on the basis of the clinical value of new antibiotics or according to specific criteria, such as whether an antibiotic has a novel mechanism of action or belongs to a new chemical class. Although the length of TEEs could be varied to account for differences in clinical value between new antibiotics, this does not completely overcome this issue. This is especially important because the majority of antibiotics in development are not considered to be innovative, and, therefore vulnerable to cross-resistance to existing antibiotics.[12]

Although TEEs can appear attractive to European Commission policy makers because of ease of implementation and incentive size, they remain a risky policy measure. Suggested improvements to TEEs, such

as auctioning based on length of patent extension to minimise potential financial costs[13] and the inclusion of access and stewardship agreements,[5] only partly address the concerns discussed above. The other option gathering momentum in Europe is the subscription-style payments to guarantee access to new antibiotics. Such incentives create a viable market for antibiotics and encourage antibiotic developers to monitor real-world effectiveness, as payments are renegotiated every 3–5 years. However, subscription-style payments would need to be implemented at the EU level and priced high enough to incentivise research and development of new antibiotics. Alongside incentives such as TEEs that target the later stages of development, it is important that governments do not overlook the need to invest in basic science and early-stage research, which is also essential to stimulate antibiotic research and development.

We declare no competing interests.

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