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A forward-looking assessment of the impact of introducing transferable exclusivity vouchers (TEV) in Europe

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1. Introduction

1.1 Background and objectives

In Europe, antimicrobial resistance (AMR) is associated with 670,000 infections and 33,000 deaths per year with these figures expected to rise as resistance continues to grow.[1] Along with the increasing burden on human health, AMR could lead to an annual decrease in European gross domestic product (GDP) of $180bn–$680bn by 2050.[2] Recognising the urgent need for new antimicrobials to combat rising resistance levels and mitigate the health and economic impact of AMR, there has been a significant debate on the global stage and in Europe about what policy interventions could effectively stimulate antimicrobial research and development (R&D).

In April 2023, the European Commission published a legislative proposal on transferable exclusivity vouchers (TEV).[3] The TEV would provide a 12-month extension of regulatory data protection (RDP) that could be used on other products in the portfolio of the antibiotic developer or sold to another company. There is widespread understanding of the value of such pull incentives as well as the cost of inaction. Over the past two years, since the publication of the initial proposal, the debate on TEV has focused on the following:[4,5]

1. **Which products the TEV will be sold and applied to** and the extent to which this sale will generate sufficient revenue to contribute to the European Union's (EU's) "fair share" of a global AMR pull incentive without overcompensating antimicrobial innovators (voiced as a key concern by several Member States)
2. **The magnitude of cost to EU Member States** and whether TEV is affordable (in terms of the incurred cost from a product getting an extra year of RDP) and whether this represents a worthwhile investment for Member States to make, proportional to the benefits of the new antimicrobial

In the Commission's 2023 Impact Assessment, the estimated value of one voucher to an antibiotic developer was €413m, at a cost to public payers of €294m per year.[6] If these costs are borne by Member States according to the relative pharmaceutical expenditure in each country, the majority of countries will pay less than €10m per TEV.[7]

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1 OECD (2019) Antimicrobial Resistance: Tackling the Burden in the European Union. Available at: https://www.oecd.org/en/publications/antimicrobial-resistance-tackling-the-burden-in-the-european-union_33cbfc1c-en.html [Accessed April 2025]

2 World Bank Group (2017) Drug-resistant infections: a threat to our economic future. Available at: https://documents1.worldbank.org/curated/en/323311493396993758/pdf/final-report.pdf [Accessed April 2025]

3 European Commission (2023) Commission proposal for the Pharmaceutical Regulation. Available at: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52023PC0193 [Accessed April 2025]

4 Berner-Rodoreda, A. et al. (2024) Transferable data exclusivity vouchers are not the solution to the antimicrobial drug development crisis: a commentary on the proposed EU pharma regulation. *BMJ Glob Health*;9:e014605. doi:10.1136/ bmjgh-2023-014605

5 Van de Wiele, V. et al. (2023) Transferable Exclusivity Vouchers and Incentives for Antimicrobial Development in the European Union. *J Law Med Ethics*; 51(1):213-216. doi: 10.1017/jme.2023.58

6 European Commission (2023) Impact assessment report and executive summary accompanying the revision of the general pharmaceutical legislation. Available at: https://health.ec.europa.eu/document/download/027a1084-0540-4bb6-b669-aa6cf3887684_en?filename=swd_2023_192_1_ia_en.pdf [Accessed April 2025]

7 CRA, EFPIA (2023) Assessing the costs of the EC's proposal for a transferable exclusivity voucher to address AMR. Available at: https://www.efpia.eu/media/ze1fqer2/assessing-the-costs-of-the-ec-s-proposal-for-a-transferable-exclusivity-voucher-to-address-amr.pdf [Accessed April 2025]

Since 2023, additional legislative restrictions have been proposed by the European Parliament and Council which would intuitively result in the cost to Member State payers being reduced further. The concern driving these restrictions has been the expectation that TEV will likely be applied to the most profitable "blockbuster" drugs and hence result in a substantial loss of cost savings for healthcare systems from delayed competition.[8] However, these estimates fail to account for how the parameters of the draft legislation will affect the number of drugs that will be eligible to apply a TEV, and the value of these medicines. To understand this, we need to take a forward-looking perspective of the medicines that could be eligible to apply a TEV when the legislation is implemented, rather than looking at products that would have been eligible in the past or today's blockbuster drugs.

The objective of this analysis was therefore to provide a forward-looking view on which product(s) a TEV could be applied to in the future when the legislation is implemented, accounting for the latest amendments to the draft legislation and considering the cost implications for Member States.

1.2 Methodology

A model was developed using a three-step approach. First, we developed a set of assumptions to account for different potential outcomes of the ongoing debate surrounding the European Commission's initial legislative proposal. Second, we generated a list of the products that would be eligible to buy a TEV from an antibiotic developer and filtered this list on the basis of these assumptions. Finally, for each of these products, the cost to Member States for the extra RDP period was estimated. This methodology is described in more detail below.[9]

1.2.1 Assumptions on the parameters of the legislation

There remains significant uncertainty regarding which elements of the European Commission's initial proposal will be brought forward into the final legislative text and which elements may still be introduced, amended or removed. Our model is based on assumptions as specified in Table 1.

Table 1: Assumptions used in the model

	Base case assumptions
In what year will the first TEV be awarded?	*2027*
At what point within a product's RDP can the voucher be used?	*Within the fifth year of RDP*
What is the expectation for the magnitude of a potential revenue cap?	*€490 million*

8 Medicines for Europe (2023) Revision of the Pharmaceutical Legislation: Position paper. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2024/01/Medicines-for-Europe-Position-paper-_-Pharmaceutical-Legislation-FINAL-1.pdf [Accessed April 2025]

9 The initial model was developed by CRA and funded by GSK. GSK reviewed the generalised results of the initial model and was involved in the decision to distribute the findings for external use by the European Federation of Pharmaceutical Industries and Associations (EFPIA). Funded by EFPIA, CRA subsequently developed the model further.

1.2.2 Generating and filtering the list of potential TEV buyers

The second step was to use the parameters listed in Table 1 to identify which products would be eligible to buy the TEV from an antibiotic developer in 2027, 2028 and 2029. GlobalData was used to identify products that were approved by the European Medicines Agency (EMA) in their first indication between January 2022 and October 2024[10] (and hence would be in their fourth, fifth or sixth year of RDP at the time of the first TEV(s) being granted in 2027, 2028 or 2029).

Multiple rounds of filtering were then conducted to identify which specific products would be most likely to buy a TEV from an antibiotic developer at different timepoints: first, products with significant patents extending beyond their RDP period were excluded;[11] then, additional filters were applied based on the assumptions in Table 1.

1.2.3 Estimating the cost to Member State payers

To estimate the financial impact of the extended RDP period to payers in Member States, we calculated the difference between the cost savings that payers could expect from generic/biosimilar competition with and without a TEV for each drug. This involved two considerations:

1. First, we estimated the speed of erosion of the originator's price and sales volume over a five-year period after loss of RDP. We developed tailored assumptions for small molecules, biologics and orphan drugs.
2. Second, we estimated the generic/biosimilar price and sales volume over the same five-year period after the originator loses exclusivity. This drew from recent analysis of post-loss-of-exclusivity trends in four European countries during 2020–2022.[12,13]

To determine the cost of TEV to payers, we compared the combined forecasted spend on the originator and generics/biosimilars for each drug over a five-year period assuming loss of RDP in year X (with no TEV) and in year X+1 (with application of a TEV resulting in an additional one year of RDP).

1.3 Comparing methodologies used to estimate the value of TEV

There are several methodological differences between the approach adopted for the European Commission's Impact Assessment, which informed the initial legislative proposal, and the approach used to generate the estimates in this study, which assumes there will be additional restrictions (as noted in Table 1).

10 The analysis was conducted in October 2024 and hence does not include additional products that may have gained EU marketing authorisation in November or December 2024.

11 Supplementary Protection Certificates (SPCs) were factored into this consideration.

12 Toghanian, S. et al. (2022) Estimating Potential for Drug Budget Reallocation Following Expiration of Exclusivity of Pharmaceutical Products. *JHEOR*. 2022;9(1):20-30. doi:10.36469/jheor.2022.29624

13 A European average of the generic/biosimilar price and volume was taken from the four countries included in the study by Toghanian et al. (weighted by pharmaceutical market size). That study only looked at the impact up to three years post-LoE; we extrapolated to year five by assuming a linear trend.

Table 2: Methodological differences between different models of TEV value

2023 Impact Assessment	This 2025 study	*Implications*
Backward-looking approach (looking at historical products as proxies for products that will be eligible in the future).	Forward-looking approach (looking at products that will be eligible in the future).	*It is important to consider the actual products that could buy and apply a TEV. A limitation of this approach is that it relies on forecasts, and actual revenues may differ.*
The cost estimate is based on the average peak revenues of a basket of products over a 10-year period (2014–2024).	The cost estimate is based on product-specific forecasted revenues (2027 onwards).	*The EU pharmaceutical market is dynamic. Average peak sales in any given year will not be representative of the sales that specific products will achieve in the future.*
The voucher can be used at any point within the first four years of RDP. The voucher will be bought by the top-selling product in a given year.	The voucher can be used only within the fifth year of RDP. The voucher cannot be applied if a product exceeds €490m annual revenue in the first four years.	*The revised legislative proposal reduces the time window within which the voucher can be applied and the limits the revenue potential of the buyer products (see Table 1); intuitively this will limit the number of eligible products that can buy the TEV.*
Commonalities across both models: The voucher is only applicable to products with RDP as their last line of protection.		

The next section of this report describes the results of this modelling; the methodological differences outlined in

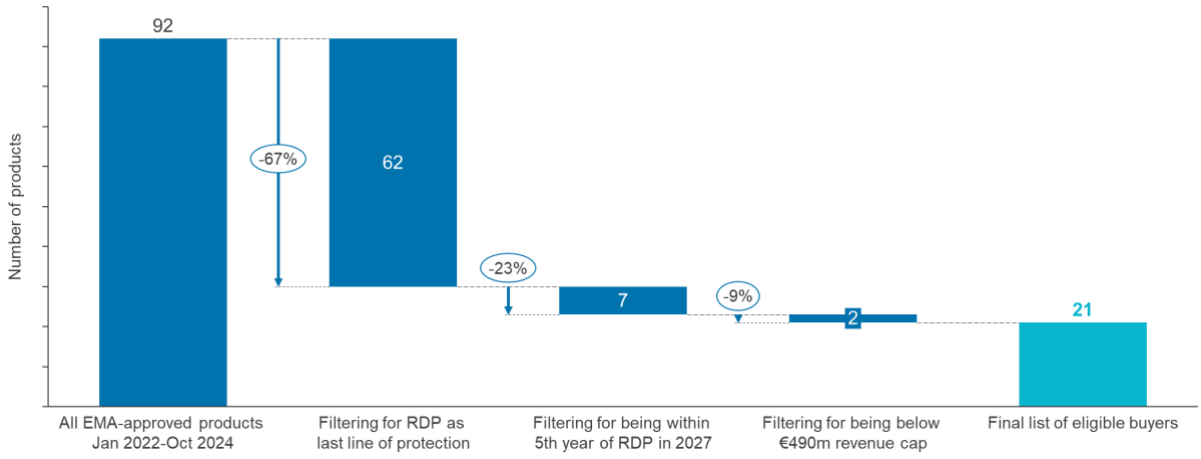
Table 2 can aid with interpretation of the results in context of existing estimates.

2. Which products could the first TEV(s) be applied to?

2.1 Results

The process for identifying products that could in theory purchase and apply a TEV is shown in Figure 1. From this modelling, we observe that the largest effect on the number of products to which the TEV can be applied is associated with the limitation of TEV to only products protected by RDP—removing 67% of the potential buyer pool. A quarter (23%) of the remaining products are removed by the restriction specifying that TEV can only be applied in the fifth year of a product's RDP. Of the products still remaining, 9% are removed from the potential buyer pool when we apply the assumption that these products cannot exceed €490m in annual sales in any of the four years prior to application of the voucher (i.e. in any of the first four years of EU marketing authorisation).

Figure 1: Identification of potential TEV buyers (base case scenario – TEV in 2027)



Source: CRA analysis

2.2 Implications for product eligibility

In all of these scenarios, only a small proportion of marketed products would be eligible to purchase and apply a TEV when the expected legislation is implemented. This has a number of implications.

There are no blockbuster products that would be able to use a TEV, even in the absence of a revenue cap. In our base case scenario, the average forecasted revenue of the 21 eligible products in their final year before loss of RDP is only €257m. The top three products in the Commission's backward-looking impact assessment had average values of €545m, €283m and €211m respectively. Limiting TEV to extending RDP limits the eligible products and means that it functions in practice as a revenue cap, and means that the TEV will not be applied to a highest-revenue blockbuster medicine. This is consistent with the Commission's Impact Assessment, which found that typically medicines with RDP as their last line of IP protection have lower average peak annual sales (€158.7m) than medicines with patents (€300.5m) or SPCs (€368.3m) as their last line of protection.

We find that the main determining factor regarding which products can use the TEV is the constraint on when the voucher can be applied in a product's lifecycle. The initial policy proposal (modelled in the Impact Assessment) provided a four-year window in which the voucher can be applied (within *the first four years* of RDP). The latest policy proposal, which we have modelled in this study, considers only a one-year window in which the voucher can be applied (within *the fifth year* of RDP,

presumably to allow the application of a cap), which significantly limits the number of products that would be eligible to buy and apply a TEV. The value of the TEV is contingent on there being the "right product at the right time". This introduces significant uncertainty for the antimicrobial developers and their investors (as during the R&D stage it will be impossible to predict the timing of EU marketing authorisations of other products with any certainty and hence predict the value of the TEV).

3. How much will Member States pay per TEV?

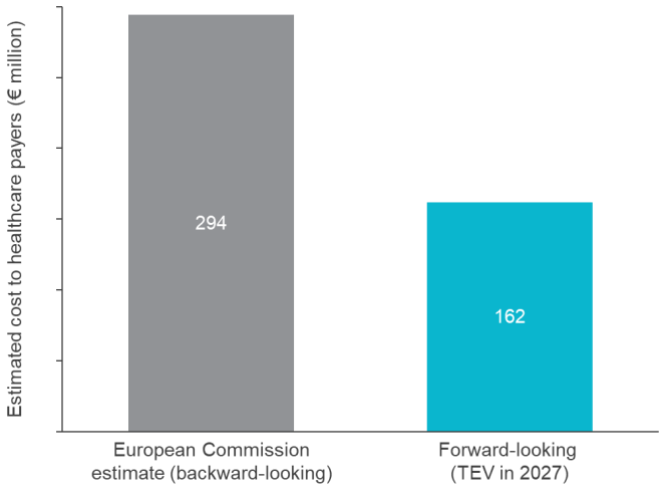
3.1 Results

There are a number of factors that would impact which of the products eligible to apply a TEV would actually purchase the voucher in practice, depending on the year and the number of TEVs. To account for this uncertainty when assessing costs of the application of TEV to healthcare payers, we therefore looked at the average cost across the top five products eligible to purchase TEVs in a given year. This is consistent with the approach used in the European Commission's impact assessment, which used average peak values obtained from a basket of products.

In our base case scenario (if TEV is implemented in 2027 and 21 products are eligible to apply it), the total cost to payers in the EU would be €162m. This is 45% lower than initially estimated with the backward-looking approach used in the European Commission's impact assessment.

These results are illustrated in Figure 2.

Figure 2: The estimated cost of one TEV applied per year in the EU



Source: CRA analysis and European Commission impact assessment (2023)

It is also important to look at the cost of a TEV to each individual Member State. This was not set out in the Commission's Impact Assessment but was estimated in a 2023 analysis, based on the total cost estimate from the Commission and allocating this to Member States based on their relative share of total EU pharmaceutical spending.[14] We replicate that approach in Table 3 using the estimated costs if TEV were to be applied in 2027.

14 EFPIA (2024) Assessing the costs of the EC's proposal for a transferable exclusivity voucher to address AMR. Available at: https://www.efpia.eu/media/ze1fqer2/assessing-the-costs-of-the-ec-s-proposal-for-a-transferable-exclusivity-voucher-to-address-amr.pdf [Accessed April 2025]

Table 3: The cost per application of TEV for each EU Member State

Member State	Estimated average cost per TEV to healthcare systems (€m)[15]	
	Based on the European Commission's EU cost estimate[16]	Based on this study's EU cost estimate (assuming TEV in 2027)
Austria	7.3	4.5
Belgium	10.3	5.6
Bulgaria	2.2	1.4
Croatia	1.5	1.0
Cyprus	0.3	0.3
Czech Republic	4.8	2.5
Denmark	4.4	2.8
Estonia	0.6	0.3
Finland	4.1	2.4
France	52.9	28.0
Germany	70.6	40.1
Greece	7.3	3.9
Hungary	5.9	2.1
Ireland	3.4	2.2
Italy	38.2	20.4
Latvia	0.4	0.4
Lithuania	1.3	0.6
Luxembourg	0.3	0.3
Malta	0.3	0.2
Netherlands	10.3	6.1
Poland	12.0	7.1
Portugal	6.6	3.3
Romania	7.3	4.6
Slovakia	2.9	1.4
Slovenia	1.0	0.7
Spain	29.4	15.5
Sweden	8.1	4.0

Source: CRA analysis

3.2 Implications of cost to Member States

One of the concerns regarding TEV is with the cost of its implementation to individual Member States.[17] The analysis above shows that the restrictions applied to TEV, in terms of limiting it to RDP, effectively

15 This approach takes data for the EU's total pharmaceutical spending and each Member State's spending to determine each Member State's respective share. This percentage share is then applied to the average total cost per TEV to identify the cost to each Member State's healthcare system.

16 EFPIA (2024) Assessing the costs of the EC's proposal for a transferable exclusivity voucher to address AMR. Available at: https://www.efpia.eu/media/ze1fqer2/assessing-the-costs-of-the-ec-s-proposal-for-a-transferable-exclusivity-voucher-to-address-amr.pdf [Accessed April 2025]

17 Member State non-paper (2022) Novel stimuli for the development and keeping on the market of antimicrobials. Available at: https://www.politico.eu/wp-content/uploads/2022/12/01/Non-paper-Transferable-exclusivity-voucher-for-AMR-2.pdf [Accessed April 2025]

reduce the cost to Member States. Other restrictions, in terms of the time constraints and application of a cap, are secondary but further limit the cost.

Looking forward to the actual products to which a TEV could be applied 2027, the average cost to an individual Member State will be €6m. Outside of the EU4 (Germany, France, Italy and Spain), every country will pay less than €7.2m per TEV. It is important to put these costs into context:

- **TEV cost relative to pharmaceutical budgets:** The cost per TEV to Member States will represent a very small percentage of their total pharmaceutical expenditure. For example, in 2022, the spend on outpatient pharmaceuticals in Spain was €12.3bn. The cost of one TEV would represent only 0.13% of this budget.
- **TEV cost relative to other approaches:** Pull incentives in other countries have advanced further along and can be used as points of reference when assessing the affordability of TEV. For example, in England, the NHS pays an annual subscription fee of £5m-£20m per eligible antibiotic for 10 years. Assuming £15m, over a 10-year period England will pay £150m (approx. €173m) per new antibiotic. This is considerably higher than the cost per TEV to any individual EU Member State.[18]
- **TEV cost relative to the cost of inaction:** The European Commission's impact assessment highlighted that it is necessary to weigh the cost of TEV against the cost of inaction and the impact of AMR on health and the economy. We can compare the cost of TEV to the estimated cost of AMR in each country to assess whether this represents a worthwhile investment to Member States. As shown in Table 4, the cost of AMR exceeds the cost per TEV. In countries with the highest burden of AMR, the benefit is even more clear; in Italy, the current cost of AMR is almost 15 times the estimated cost of one TEV. Even in smaller Member States with a lower burden of resistance, such as Denmark, the cost of AMR still exceeds the cost of a TEV.

Table 4: Cost per TEV relative to cost of AMR

Member State	Estimated average cost per TEV (€m) (assuming TEV in 2027)	Estimated annual cost of AMR (€m)[19]
Austria	4.5	16.1
Belgium	5.6	22.0
Bulgaria	1.4	4.1
Croatia	1.0	5.5
Cyprus	0.3	2.6
Czech Republic	2.5	16.8
Denmark	2.8	4.10
Estonia	0.3	0.3
Finland	2.4	2.2
France	28.0	264.3
Germany	40.1	134.1
Greece	3.9	42.6
Hungary	2.1	15.5

18 It is important to note that England's subscription model is generally considered to represent a "fair share" UK contribution to a global pull incentive, whereas estimates of the value of TEV fall short of an EU "fair share" contribution.

19 Consistent with CRA (2024), our approach to identifying the annual cost of AMR leverages OECD data on the per capita cost of AMR and current population numbers for each Member State.

Ireland	2.2	14.1
Italy	20.4	298.9
Latvia	0.4	0.9
Lithuania	0.6	2.0
Luxembourg	0.3	2.6
Malta	0.2	4.1
Netherlands	6.1	10.6
Poland	7.1	65.6
Portugal	3.3	47.2
Romania	4.6	23.9
Slovakia	1.4	15.6
Slovenia	0.7	3.2
Spain	15.5	76.9
Sweden	4.0	4.2

4. Conclusion

The new modelling presented in this study suggests that the cost of TEV to EU Member States will be lower than initially estimated at the time of the European Commission's first legislative proposal. This is because we have undertaken a forward-looking assessment (and this lowers the average value of products) and updated the eligibility criteria based on the latest legislative proposal (with constraints due to RDP and timing), narrowing the selection of products to which the TEV could be applied to in practice. In the Commission's modelling they used historically top-selling products.[20,21]

It is important to acknowledge that while the restrictions proposed to the draft TEV legislation by the European Parliament and Council may result in lower costs to Member States, they will also weaken the value of TEV to antimicrobial developers and hence weaken the incentive. These results also mean that TEV alone will be unlikely to provide an incentive of sufficient scale. A broader complementary package of incentives is needed to deliver the EU's estimated fair share of a global pull incentive.

20 European Commission (2023) Impact assessment report and executive summary accompanying the revision of the general pharmaceutical legislation. Available at: https://health.ec.europa.eu/document/download/027a1084-0540-4bb6-b669-aa6cf3887684_en?filename=swd_2023_192_1_ia_en.pdf [Accessed April 2025]

21 Medicines for Europe (2023) Revision of the Pharmaceutical Legislation: Position paper. Available at: https://www.medicinesforeurope.com/wp-content/uploads/2024/01/Medicines-for-Europe-Position-paper-_-Pharmaceutical-Legislation-FINAL-1.pdf [Accessed April 2025]

Abbreviations

AMR	antimicrobial resistance
EMA	European Medicines Agency
EU	European Union
GDP	gross domestic product
IP	intellectual property
R&D	research and development
RDP	regulatory data protection
SPC	supplementary protection certificate
TEV	transferable exclusivity voucher(s)

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