Market Concentration of New Antibiotic Sales

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Abstract

We calculate the average sales of new antibiotics during their first eight years on the market. The discounted net present value is only $240m in total per antibiotic, well below costs of supplying these products. The reliance on the US for sales is striking: the US market accounts for 84% of sales during the first 8 years. These facts clarify the need for additional revenues, especially from other countries, to support incentives for the development of new antibiotics. Market entry rewards may be of particular value.

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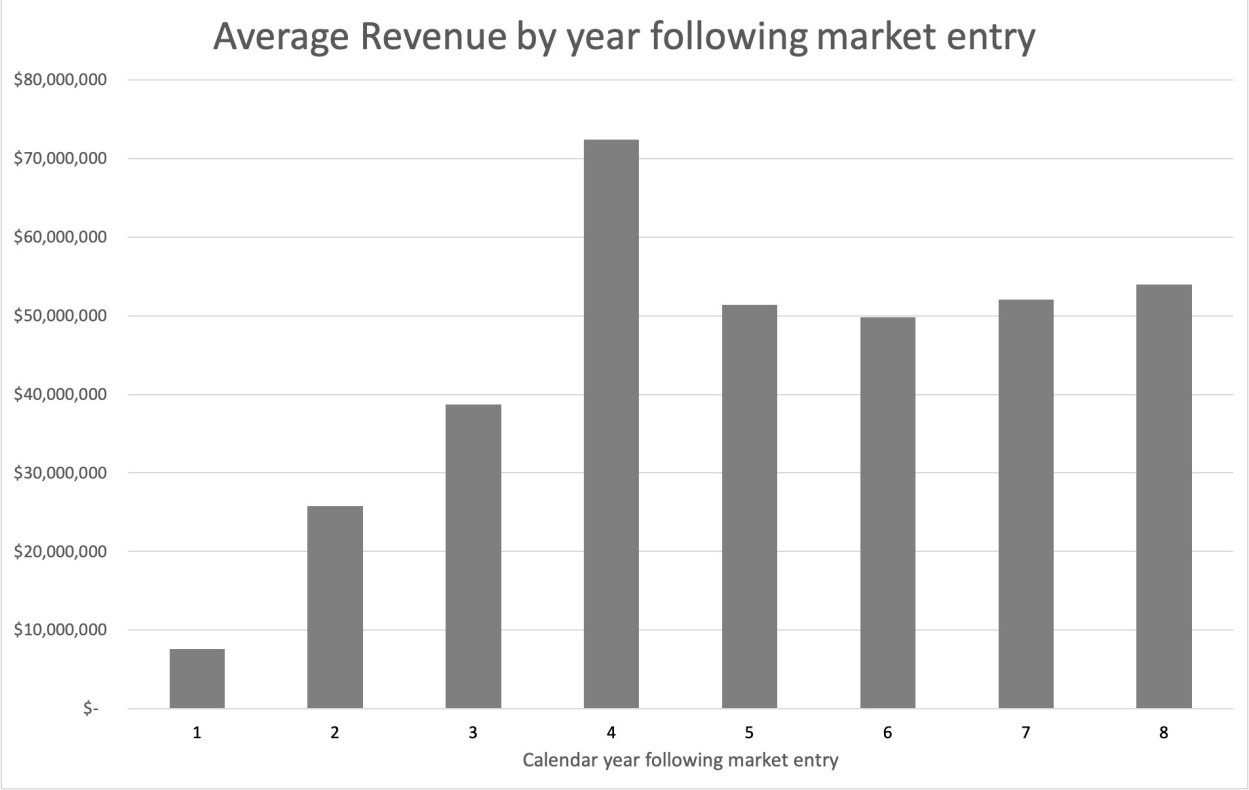
The commercial challenges of new antibiotics are well known (1,2). Numerous solutions have been proposed, including the grant model applied by CARB-X and BARDA, market entry rewards, and reimbursement models (3,4). In this paper, we point out that there is both a money problem and a lack of geographic diversity in markets, which are likely connected.

Using data from IQVIA, we calculated sales of new antibiotics. We identified all antibiotics in the IQVIA data that had their first identified sales between 2008 and 2018, of which there were 16. Several of these were introduced at relatively low prices, such as antofloxacin, which recorded sales only in China. We excluded all antibiotics with a revenue of less than $20 per defined daily dose, which left us with 10 molecules.[1] The average revenue per defined daily dose for these 10 molecules was $275, so they were much more expensive than typical generic antibiotics.

Our data included 46 countries, representing all major pharmaceutical markets. Since each antibiotic entered at a different time, we ordered them by years since entry, and then calculated the average revenue per drug during each year, as shown in Figure 1. Our data ends in 2018, so we have data for multiple drugs only up to 8 years following entry. The year of entry (shown as year 1 in Figure 1) represents only a partial year of sales. We see an increase in sales as products become established in the market. The average revenue per product over the first 8 calendar years of sales has a net present value at market entry of only $240m, assuming a cost of capital of 10%.

[1] Avibactam Ceftazidime, Ceftaroline Fosamil, Ceftobiprole modecaril, Ceftolozane, Dalbavancin, Delafloxacin, Meropenem vaborbactam, Oritavancin, Tedizolid, and Telvancin.

These revenues compare unfavorably to the costs of supplying antibiotics to the market. Post-marketing studies, surveillance, medical affairs, and antimicrobial susceptibility testing for new antibiotics are estimated to cost between $92m and $222m (depending on product complexity) in the five years following product launch.(5) This does not account for *any* pre-approval costs such as research and development and regulatory submissions, or other post-launch costs such as manufacturing (which could be expected to cost in the range of $250m in the first five years) and liability.(6) In effect, antibiotic revenues are too small to cover the post-launch costs, let alone costs of development, which are estimated to range from $985m to $1336m (7).



What is most striking is the extent to which the sales of these products are geographically concentrated. We calculated for the same set of 10 molecules the revenues by income category: High-Income (HIC), Upper Middle-Income (UMIC), and Lower Middle-Income (LMIC), using the World Bank categorization of countries (8). The IQVIA data did not include any Low-Income countries. However, our expectation is that given the tiny sales in Lower Middle-Income countries, the sales in Low-Income countries would be minimal. We split out the United States (US) from other High-Income countries. The revenue shares are as shown in Figure 2. Lower Middle-Income country sales are visible only in years 3 and 4.

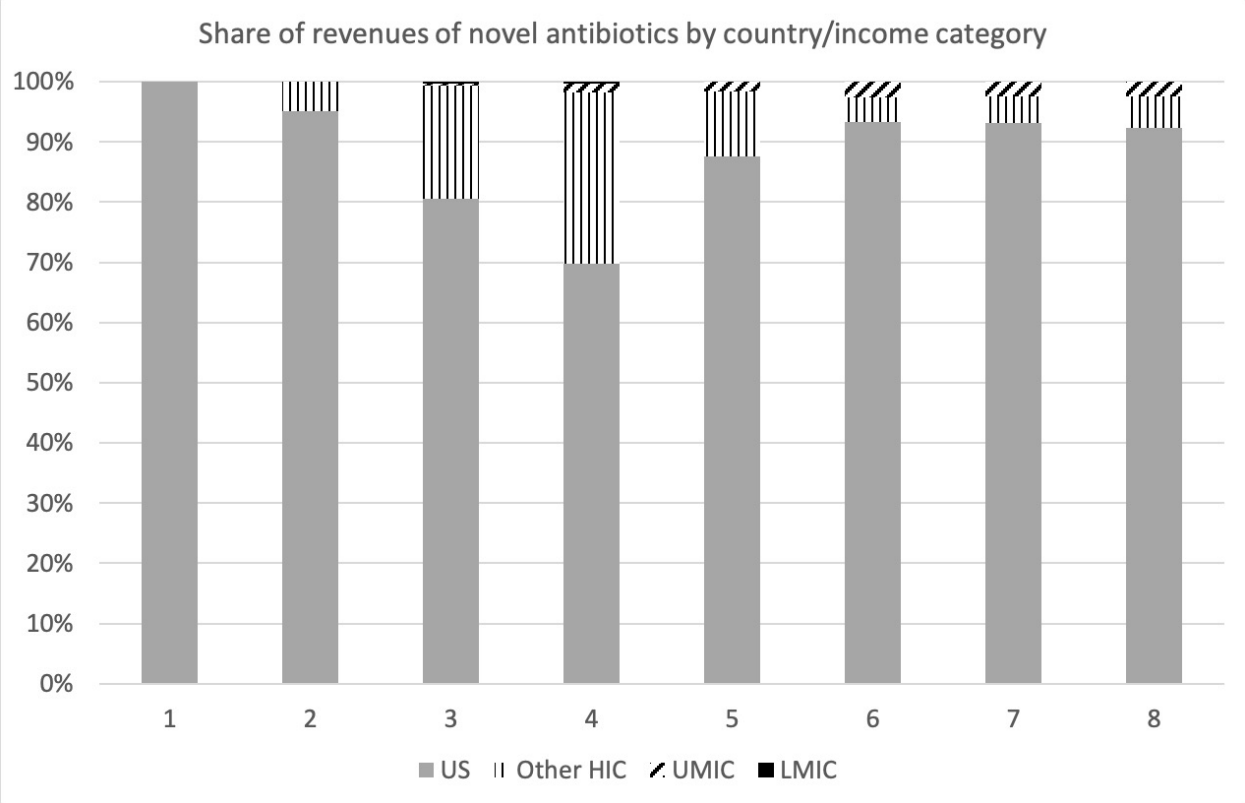


Figure 2 clarifies that revenues from new antibiotics almost exclusively come from High-Income countries. Moreover, the US, with 4% of the global population, represents fully 84% of sales of these products during the first 8 calendar years following market entry. This dependence on the US is unhealthy and helps to explain why total product revenues are so small: essentially, there is very little penetration of other markets that offer the potential to increase sales volumes considerably. The near-exclusive focus on the US is particularly unwelcome since the average level of resistance in the US is relatively low, compared to many other markets where the need for newer antibiotics is greater.(9)

The reason for the commercial focus on the US market is not hard to identify: US prices tend to be higher, and there is greater willingness on the part of hospitals and insurers to pay for high-priced novel antibiotics.(10) This leads to earlier submissions and earlier approvals. For example, Ceftazidime-avibactam was submitted for approval to the FDA in June 2014, and the EMA in March 2015. It has yet to be submitted for approval in Canada. Dalbavancin was submitted to the FDA in November 2013, to the EMA in November 2013, and to Health Canada in March 2018.[2]

The result of the dependence on the US market is that firms, relying on relatively low levels of resistance in the US, do not earn the profits that could come from higher sales in countries with greater measured resistance and greater clinical need for these newer antibiotics.

[2] See https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2015/206494Orig1s000ltr.pdf, https://www.ema.europa.eu/en/documents/assessment-report/zavicefta-epar-public-assessment-report_en.pdf, https://www.drugs.com/nda/dalvance_140401.html, https://www.ema.europa.eu/en/documents/assessment-report/xydalba-epar-public-assessment-report_en.pdf, https://www.ema.europa.eu/en/documents/assessment-report/xydalba-epar-public-assessment-report_en.pdf, all accessed 14 November 2020.

Considering the low sales revenues of new antibiotics, and the heavy reliance on the U.S. market of these sales, if any more drugs are to be developed either costs must be subsidized or revenues must be augmented by other means. A much-discussed way of increasing revenues is through Market Entry Rewards or fixed payments granted once a new antibiotic is approved for clinical use.

The new Market Entry Reward scheme piloted in the United Kingdom offers payments for qualifying products that could be up to GBP 100m during the first ten years, which would increase the global revenues of the average novel antibiotic by about 50% (11). If other countries were to join such a scheme, the cumulative effect on the market could possibly create the necessary "pull" needed to support investment in new antibiotics. However, while Market Entry Rewards may top-up the revenue shortages of new antibiotics to make them profitable, adding incentives for stewardship would strengthen the ability of such a reward to target long-term effective molecules as well as support the prudent level of marketing and use of the new drug (12).

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