Supplemental Online Content

Tu SS, Nagar S, Kesselheim AS, Lu Z, Rome BN. Five-year sales for newly marketed prescription drugs with and without initial Orphan Drug Act designation. *JAMA*. Published May 9, 2023. doi:10.1001/jama.2023.3079

eApppendix. Supplemental Methods

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix. Supplemental Methods

Newly Marketed Drugs

Newly marketed brand-name drugs from 2008 to 2016 were identified using the same method as previously described.[1] Drugs were first identified using SSR Health, a database that contains data on 1230 brand-name products made by public companies.[2] The date of market entry was determined primarily based on the first quarter of available data in SSR Health; in cases when this occurred 1 year or more after US Food and Drug Administration approval, we used an industry database (IBM Red Book) to verify and correct, if necessary, the date of market entry.

Net Sales

We obtained quarterly net sales data from SSR Health, which collects this information from public quarterly manufacturer financial reports. Companies report product-level sales net of any price concessions, including rebates to payers and pharmacy benefit managers.

We reviewed drugs with missing quarterly data during the first 5 years on the market and manually reviewed quarterly financial reports to fill in any additional data that were available. Companies typically report sales only on their highest-selling products, so in cases where sales were not reported we assumed zero sales. Four drugs had no reported sales in the first 5 years; in these cases we rounded to a nominal amount of $100,000 so that these could be included in the log-transformed model.

Orphan Designation

We classified drugs as orphan-designated if they were initially approved by the FDA for only orphan designated indications. To determine this, we searched the FDA's Orphan Drug Designations and Approvals to identify all indications granted an orphan designation for each drug, as well as the date of the designation.[3] Drugs without any orphan designations were assumed to be non-orphan. For those with 1 or more orphan designation, we compared these designations against the indications listed on each drug's originally approved FDA labeling from Drugs@FDA. [4] We classified drugs as orphan-designated only if the drug's original indication was granted an orphan designation prior to FDA approval. In cases where drugs had multiple initial indications, we only classified drugs as orphan-designated if all the indications were orphan-designated. We classified 6 drugs that had both orphan-designated and non-orphan indications as non-orphan, because we assumed that pricing decisions and sales during the first 5 years would be based on the more common, non-orphan indication(s).

For orphan-designated drugs, we reviewed all indications added to the drug's labeling within the first 5 years using Drugs@FDA. Each indication was compared to the drug's orphan designations. This allowed us to determine whether drugs that were initially approved for an

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[1] Rome BN, Egilman AC, Kesselheim, AS. Trends in Prescription Drug Launch Prices, 2008-2021. JAMA: 2022; 327(21): 2145-2147.

[2] Hernandez I, San-Juan-Rodriguez A, Good CB, Gellad WF. Change in list prices, net prices, and discounts for branded drugs in the US, 2007-2018. JAMA 2020; 323(9): 854-862.

[3] https://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm

[4] US Food and Drug Administration. Drugs@FDA: FDA-Approved Drugs. Accessed January 26, 2023. https://www.accessdata.fda.gov/scripts/cder/daf/

orphan indication were subsequently granted approval for a non-orphan indication in the subsequent 5 years. These “cross-over” drugs were still included as orphan-designated in the primary analysis because they still benefit from the financial incentives under the Orphan Drug Act and the pricing and marketing decisions were initially based on an orphan-designated indication.

We also identified 10 drugs with multiple orphan-designated indications. Each orphan designation refers to a patient population of up to 200,000 people in the US, so drug with 2 or more orphan designations could be indicated to treat a larger population.