CostPlus and implications for generic imatinib

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In January 2022, American billionaire Mark Cuban opened the Cost Plus Drug Company (CPDC)[1] —an online pharmacy offering >100 generic medicines at more affordable prices. Although patients pay out of pocket (the company does not process insurer claims), list prices are significantly less compared to other insurance plans.

A new option for buying prescription drugs in a market prone to shortages and unjustifiable price increases[2] has been met with an overwhelming positive reception from health professionals, patients, and the media.[3] However, since the company sells generic medicines, it will be limited to what medicines it can supply to patients. We consider the company's first foray into cancer drug pricing: the anti-cancer drug imatinib (Gleevec) to highlight market challenges for generic medicines and to underscore the limits of private-sector innovation to address high prices of cancer drugs in the United States (US). Given the dominance of the US pharmaceutical market, we argue that these market failures have global implications and genuine "disruption" to the US health care system can only happen with government leadership.

Imatinib is a tyrosine kinase inhibitor (TKI) licensed for use in several conditions such as chronic myelogenous leukaemia (CML) and remains one of the most effective cancer treatments ever developed. The CPDC charges $47 for a month supply of 400mg tablets — a nearly 99% price reduction beyond other generics (Figure 1A).[1] The company accomplishes this by purchasing generic drugs directly from several manufacturers and selling them with small markups that include a flat 15% margin, and a $3 pharmacist fee. However, the CPDC is subject to US market challenges that impact access to generic medicines in the US and globally.

First, the introduction and promotion of second-generation products contributes to suboptimal use of existing generic drugs within the US. Imatinib (Novartis) came to the US market in 2001. In 2006 and 2007, it was joined by nilotinib (Novartis) and dasatinib (Bristol-Meyers Squibb). These newer drugs have never shown longer survival or better quality of life but have rapidly gained market share because they can induce deeper molecular responses.[4] By the time generic imatinib entered the market in 2016, imatinib was no longer the preferred option. Over 60% of CML patients were starting with nilotinib and dasatinib. Thus a generic, at best, could only apply for 40% of patients, and the reality was it only accounted for only 28 percent[5] (Figure 1B). For highly successful "blockbuster" drugs, such as imatinib, companies often develop similar products prior to patent expiration and attempt to shift prescribing behaviours through extensive marketing campaigns[6] Despite the availability of generic imatinib, increased use of nilotinib and dasatinib resulted in higher patient spending overall.[5]

Second, pharmaceutical manufacturers often use a variety of laws to safeguard US drug patents which delay market entry of generic drugs. Chen et al. outline various mechanisms Novartis used to extend the US patent on imatinib from an original expiration date of May 2013 to November 2019.[6] By applying for patent term restoration, paediatric exclusivity, and secondary patents on additional formulations of imatinib, Novartis was able to gain an additional six years of market exclusivity without offering any additional survival benefit to patients. At the same time, the price of brand name imatinib more than doubled from $4000 in 2001 to nearly $10,000 per prescription fill in 2015.[5] Given barriers to cheaper, conventional chemotherapies in low and middle income countries (LMICs),[7] the delay for generic imatinib likely had deadly consequences for patients who could not afford high-priced patented alternatives.

Third, the uptake of second-generation products and delayed entry of generic pharmaceuticals often creates insufficient incentives for market competition. Anticancer drugs are some of the most expensive medicines and few have generic options. In a recent poll, 18 million Americans (7%) reported they could not pay for one prescribed medication and 1 in 10 reported skipping a dose to save money.[8] Similarly, drug prices in Latin America have risen in parallel with the US. In Argentina, the average cost of cancer medicines is now $17 700 per month.[9] Similar trends are observed in Brazil, Ecuador, and Colombia.[10] The story of CML demonstrates that by the time the parent compound was eligible for generic entry, the field had substantively moved to second-generation compounds. This is true in other spaces in

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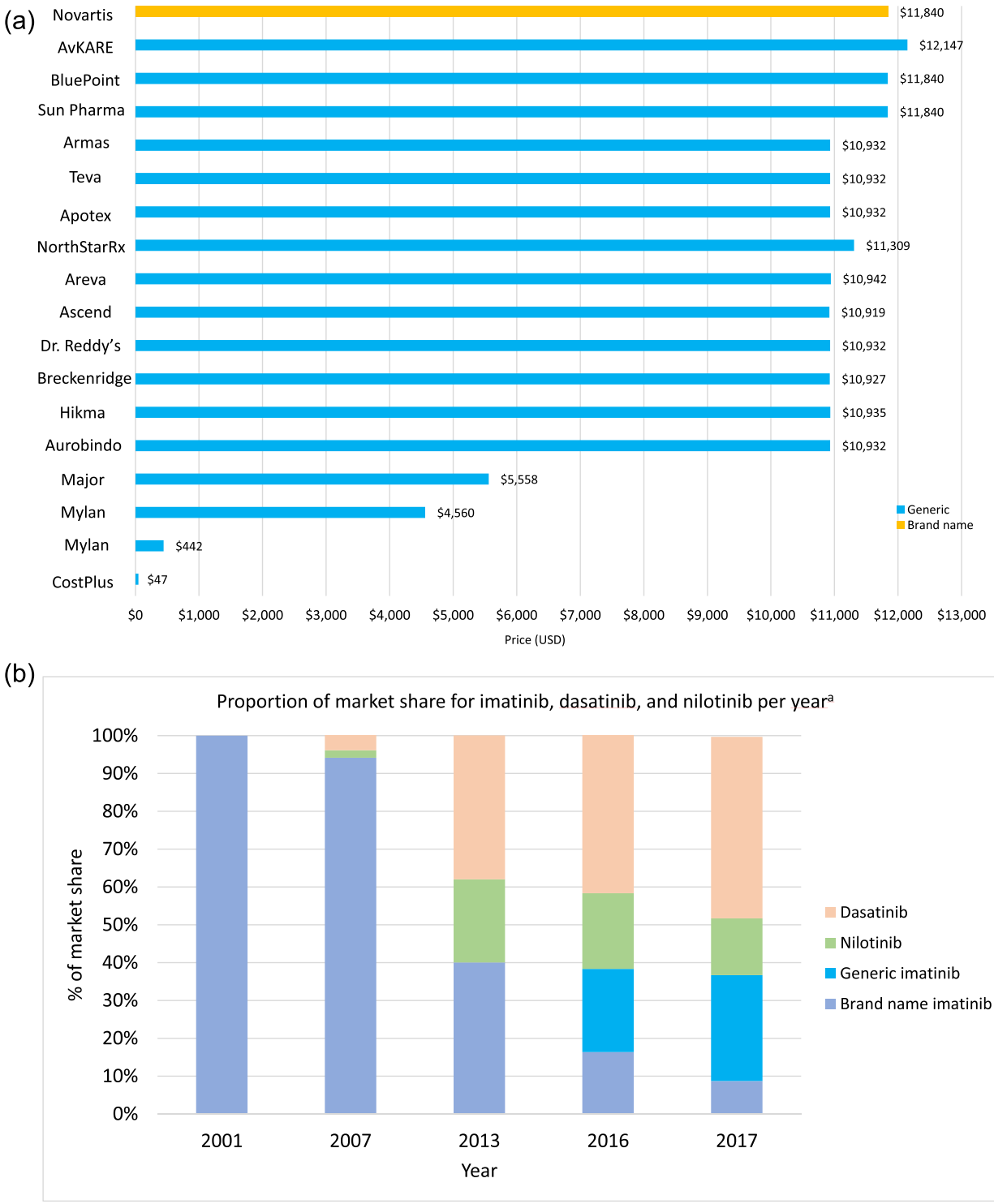

Figure 1. (A) Price of imatinib for an average one-month supply (400mg tablets) per manufacturer. (B) Proportion of market share for imatinib, dasatinib, and nilotinib per year[a].

[a]Figure adapted from Cole & Dusetzina (2018).

oncology, including EGFR inhibitors for lung cancer, Tyrosine-Kinase inhibitors for kidney cancer, and Bruton Tyrosine Kinase Inhibitors in lymphoma.

The US government has tools at its disposal to reduce drug costs now. The Biden Administration could pass the Build Back Better (BBB) bill which included provisions to cap out-of-pocket spending for seniors and enable Medicare to negotiate with pharmaceutical manufacturers. However, the scope of the BBB bill has narrowed to a subset of 10 drugs and its fate in Congress has weakened. Beyond the BBB bill, the government could exercise laws outlined within the Bayh-Doyle and Hatch-Waxman Acts to streamline the process for generic approvals.[11]

Contributors

Ms. Jenei led the manuscript development and submission in collaboration with Drs. Prasad and Lythgoe. All authors were involved in conceptualization, methodology, validation, writing, reviewing, and editing the manuscript. In addition, Ms. Jenei conducted data analysis using REDBOOK with validation from Drs. Prasad and Lythgoe.

Declaration of interests

Dr Prasad reports research funding from Arnold Ventures, royalties from Johns Hopkins Press, MedPage, YouTube, Substack, consulting for Optum Health, and contributions from Patreon backers for Plenary Session podcast. Dr. Lythgoe has received advisory fees from Clovis Oncology outside the submitted work. Ms. Jenei reports no conflicts.

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