

# Pricing of Monoclonal Antibodies in the United States

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## INTRODUCTION

Rising pharmaceutical prices have been a growing concern for providers, payers, patients, and policymakers around the world, but these are a particularly pressing matter in the United States (US) where pharmaceutical prices are not regulated. Specialty medications are a prominent driver of the rising costs of prescription drugs in the US and currently account for as much as 40% of pharmaceutical spending.<sup>[1-4]</sup> With the average price of a cancer drug doubling in the last decade,<sup>[1,5]</sup> the unsustainability of specialty drugs has drawn special attention in the oncology field.<sup>[1,5-9]</sup> Yet, little is known about how drug prices compare across therapeutic areas, and whether specialty drugs used in cancer are actually more expensive than specialty drugs used in other disease states. An article recently published in the *American Journal of Managed Care* sheds some light into this issue. In this piece, Hernandez *et al.* examined the prices of all monoclonal antibodies approved by the US Food and Drug Administration (FDA) in the last 20 years (from 1997 to 2016) to find that the average annual price of monoclonal antibody therapies was \$96,731.<sup>[10]</sup> After adjusting for factors that can affect production costs, the prices of monoclonal antibody therapies used in cancer were found to be around \$100,000 more expensive than those used in other disease states.<sup>[10]</sup> Even if monoclonal antibodies used in hematology and oncology only represented 40% of the total number of monoclonal antibodies approved by the FDA in the last 20 years, they accounted for over 85% of the monoclonal antibodies, with an annual price of treatment exceeding \$100,000 per person.

## FACTORS FOR DIFFERENTIAL PRICING ACROSS DISEASE STATES

Several factors may explain the higher prices of monoclonal antibody therapies used for cancer treatment. First, in order to recover the fixed costs of research and development, manufacturers often set higher prices for drugs used in conditions with low prevalence, and the types of cancer treated by monoclonal antibodies are generally less prevalent than other diseases.<sup>[11]</sup> Treatment duration plays a similar role on the pricing of drugs: while most hematology and oncology treatments do not last longer than a couple of months, chronic diseases treated by monoclonal antibody treatments such as arthritis and other inflammatory conditions often require lifelong medication use. Therefore, manufacturers

will be more likely to set higher prices for therapies that require shorter treatment duration when compared to monoclonal antibody therapies used in long-lasting indications. Second, antineoplastic agents are one in eight Medicare Part D-protected drug classes, which implies that Medicare Part D plans are required to cover all drugs indicated in the treatment of cancer.<sup>[12]</sup> In addition, many states also require private insurers to cover antineoplastic drugs.<sup>[13]</sup> Since payers are required to cover all cancer drugs by law, they have little leverage over the price of these therapies. These regulations can also explain why prices for monoclonal antibodies used to treat cancer are higher compared with specialty drugs used to treat other disease states, such as PCSK9 inhibitors used in hypercholesterolemia or monoclonal antibodies used in osteoporosis. Finally, since drug pricing in the US is driven by the principles of free market, prices reflect the market's willingness to pay for a product rather than its production costs or its value. Since cancer is the most feared disease by Americans,<sup>[12]</sup> the society may be willing to pay more for the treatment of cancer than for the treatment of other conditions, which results in higher prices for drugs used in cancer.

## IMPACT OF BIOSIMILARS ON MONOCLONAL ANTIBODY PRICING

In addition to the substantial differences observed in the pricing of monoclonal antibodies across disease states, the average annual price of monoclonal antibody therapies and the potential impact of new biologics also deserve comment. With a reduced range of companies manufacturing a small number of specialty drugs, a *de facto* oligopoly has been developed where higher prices can be set by selected manufacturers. However, the Biologics Price Competition and Innovation Act of 2009 opened the door to increased competition by facilitating the development and FDA approval of biosimilars.<sup>[14]</sup> Through December 2017, the FDA has approved nine biosimilar products (Zarxio<sup>®</sup>, Erelzi<sup>®</sup>, Inflectra<sup>®</sup>, Amjevita<sup>®</sup>, Renflexis<sup>®</sup>, Cyltezo<sup>®</sup>, Mvasi<sup>®</sup>, Ogivri<sup>®</sup>, and Ixifi<sup>®</sup>) of filgrastim, etanercept, infliximab, adalimumab, bevacizumab, and trastuzumab.<sup>[15]</sup> The introduction of

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biologics in the filgrastim market illustrates an interesting case on how biologics may transform access and costs of specialty drugs. Granix<sup>®</sup>, a filgrastim biologic that was submitted for FDA approval before a biosimilar pathway was established, entered the market in late 2013; while Zarxio<sup>®</sup>, an FDA-approved biosimilar of Amgen's Neupogen<sup>®</sup> that is manufactured by Sandoz, entered the market in September 2015. These new entries to the filgrastim market have led to substitution from Neupogen<sup>®</sup> to Granix<sup>®</sup> and Zarxio<sup>®</sup>. In December 2016, Granix<sup>®</sup> and Zarxio<sup>®</sup> together represented 30% of the filgrastim market share by sales and almost a 43% by volume.<sup>[4,15]</sup> More importantly, these market entries were associated with cost savings. Specifically, after the market entry of Granix<sup>®</sup> and Zarxio<sup>®</sup>, net sales of filgrastim products dropped from \$931 million in 2013 to \$766 million in 2016.<sup>[15]</sup> Even though Neupogen<sup>®</sup> has maintained a practically constant price since 2013, the substantial reduction in sales observed in 2016 was likely because Granix<sup>®</sup> and Zarxio<sup>®</sup> were offered at prebate prices 30% and 45% lower, respectively, than their reference biopharmaceutical Neupogen<sup>®</sup>.<sup>[15]</sup> Nonetheless, with only three biosimilars commercially available at this time (Zarxio<sup>®</sup>, Inflectra<sup>®</sup>, and Renflexis<sup>®</sup>), there is still scarce evidence about the comprehensive impact of biosimilars in the US health market. As new biosimilars indicated in a wide array of conditions become available, it will be important to examine whether this increased competition will increase access to specialty drugs and lower pharmaceutical spending.

### POLICY RECOMMENDATIONS

In brief, price differences of biological products across diverse disease states cannot be fully explained by research, development, or production costs. Drug pricing lacks transparency and may be affected by factors such as varying treatment duration, legal requirements for coverage for certain disease states, and increased willingness to pay for specific indications such as cancer. In the future, it will be important to increase the transparency of the price fixing process, as well as to develop some type of value framework that ensures that the reimbursement of innovative products is truly aligned with actual quantifiable benefits of pharmaceuticals, rather than with the societal perception of the novel therapies. In addition, as new biosimilars indicated in a wide array of conditions become available, it will be important to examine whether increased competition will decrease prices and improve access to these specialty medications. The time has come for us, as a society, to pursue a pharmaceutical pricing system that allows for transparency and sustainability of pharmaceutical coverage by public payers.

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