Attachments—Additional Questions for the Record

Subcommittee on Health
Hearing on
"Lowering Prescription Drug Prices: Deconstructing the Drug Supply Chain"
May 9, 2019

Kave Niksefat

The Honorable Joe Kennedy

Mr. Niksefat, during my questions to you at the Subcommittee hearing, I asked how Amgen sets the list price for medication, specifically Neupogen, and why there is significant variation in price between the United States and Denmark, two countries without government price controls. I would like to use this opportunity to allow you to clarify your responses to my questions.

1. When I asked if it is appropriate for Amgen to continue to charge American taxpayers for your company's research risks, on the back of an old product, you responded, "Neupogen is subject to direct biosimilar competition, and that biosimilar competition now has the vast majority of the market share".

   However, Neupogen faces biosimilar competition from only one biosimilar product: Zarxio, and another biologic drug, Granix. If we define "market share" by the percentage of total sales (in dollars) captured by the product, Neupogen remains in the lead. According to a February 19, 2019 article in the Journal of Clinical Pathways, Neupogen has 48 percent of the market share, and Zarxio has 31.7 percent. Granix has only 20.3 percent.

   Therefore, I again ask, it is appropriate for Amgen to continue to charge American taxpayers for your company's research risks, on the back of an old product? Furthermore, do you still contend that biosimilar competition has the "vast majority" of the market share? If so, please explain.

Amgen strongly supported the bipartisan Biologics Price Competition and Innovation Act (BPCIA), which established a pathway for the entry of biosimilar competition in the U.S., as well as a patent litigation structure and data exclusivity protections for biologics. Amgen embraced the opportunity to bring more affordable biologics therapies to U.S. consumers. We currently have ten biosimilars in our portfolio, including two oncology biosimilars that we launched in the U.S. in July 2019. Amgen uses revenues of its approved biologics (including NEUPOGEN® (filgrastim) and our own biosimilars) to support the research and development of new therapies; Amgen invested $3.66 billion in research and development in 2018 and close to

$19 billion over the past five years.[1]

NEUPOGEN has faced more intense competition in the U.S. since late 2013, with the introduction of GRANIX® (tbo-filgrastim) and biosimilar competition beginning in late 2015 with the launch of ZARXIO® (filgrastim-sndz). Amgen expects additional competition in this market through at least one more biosimilar competitor which launched in late 2018.

As of July 2019, NEUPOGEN had approximately 32 percent unit share of U.S. short acting granulocyte colony stimulating factors (GCSFs).[2] Based on gross sales, NEUPOGEN had 35 percent of share in the U.S.[3] ZARXIO gross sales in the U.S. have been exceeding NEUPOGEN since Q3 2018 and combined ZARXIO and GRANIX gross sales exceeded NEUPOGEN gross sales since mid-2017.[4]

Other analysts have reported similar findings. A recent Bernstein Research report based on IQVIA data through April 2019 states "US biosimilar adoption of Neupogen is progressing well, with biosimilars reaching 60 percent of the molecule by volume."[5] In written testimony submitted earlier this year to the Subcommittee on Health of the House Committee on Energy and Commerce, the Executive Director of the Medicare Payment Advisory Commission (MedPAC) stated "…utilization has shifted away from the more costly originator biologic Neupogen, with its biosimilars accounting for 63 percent of the market in the first quarter of 2018."[6]

2. Additionally, when I stated "…since competitive entry of Granix in 2012 and Zarxio in 2015, Neupogen's price has risen and is still the market share leader in both total revenue and unit volume," you stated, "It is not the case in unit volume… Neupogen unit volume, if I remember correctly, is approximately below a third of the entire market."

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[1] Amgen 2018 Letter to Shareholders, p.2, p10. Available at http://investors.amgen.com/static-files/e3bd5ffc-957d-4dac-a8b4-5ed9a9a34e94.

[2] Amgen data on file. Methodology: Calculation of unit share is based on units sold for the following products in the short acting GCSF market basket: NEUPOGEN, ZARXIO, GRANIX, NIVESTYM™ (filgrastim-aafi), and LEUKINE® (sargramostim) (note, ZARXIO and NIVESTYM are biosimilars). The analysis is based on IQVIA DDD® data, supplemented with Amgen proprietary data and estimates for select customer segments not included in IMS DDD. Because IQVIA DDD is not 100 percent complete, Amgen uses proprietary data and estimates to fill gaps.

[3] Amgen data on file. Methodology: Calculation of share by gross sales is based on units sold times wholesale acquisition cost (WAC) for the following products in the short acting GCSF market basket: NEUPOGEN, ZARXIO, GRANIX, NIVESTYM, and LEUKINE. The analysis is based on IQVIA DDD data, supplemented with Amgen proprietary data and estimates for select customer segments not included in IMS DDD. Because IQVIA DDD is not 100 percent complete, Amgen uses proprietary data and estimates to fill gaps.

[4] Ibid.

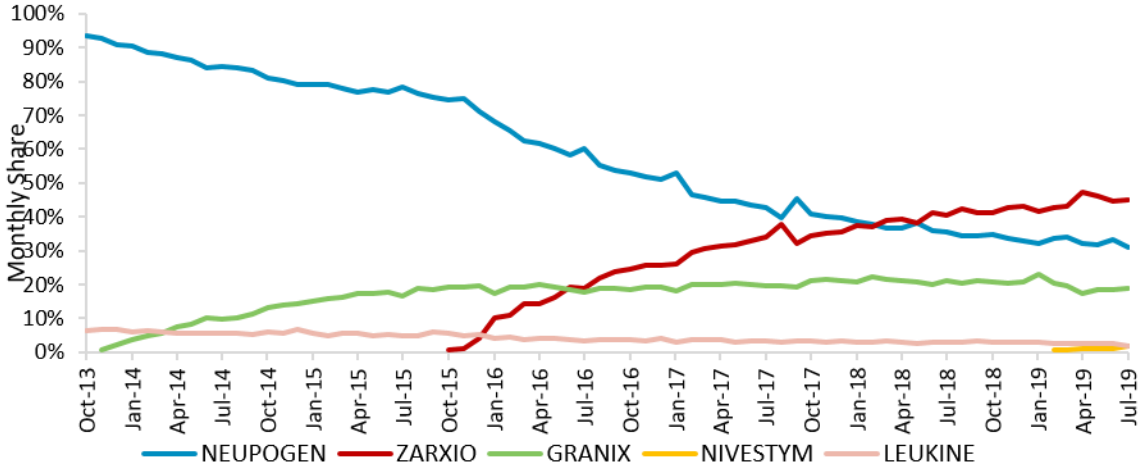
[5] Bernstein Research Report. Biosimilars in EU & US - Apr-May data; EU Humira market growth, EU oncology tracking stronger, material price impact in US, p. 28 (July 10, 2019). Note: Report states this includes one true biosimilar (ZARXIO) and one value brand (GRANIX).

[6] Statement of James E. Mathews, Ph.D., Executive Director, MedPAC, before the Subcommittee on Health, Committee on Energy and Commerce, U.S. House of Representatives, p.14 (April 30, 2019). Available at https://energycommerce.house.gov/sites/democrats.energycommerce.house.gov/files/documents/MedPAC_Testimony_for_EandC_04_30_2019.pdf.

However, it is my understanding the sales volume of Neupogen and Zarxio are quite similar. Please describe the current sales of Zarxio, Granix, and Neupogen in sales volume and revenue, and then clarify your statement that "biosimilar competition now has the vast majority of the market share." Specifically how do you define "vast majority"?

Available data indicate that our competitors have a majority of both the unit share and gross sales. As mentioned in my response your first question, as of July 2019 NEUPOGEN unit sales share is 32 percent compared to biosimilar and biologic competitors which combined have more than double the short acting GCSF unit sales.[7] See Figure 1 below for monthly unit share since October 2013.

Figure 1: Short Acting GCSF Monthly Unit Share[8]



Based on gross sales, as of July 2019 NEUPOGEN had 35 percent of share in the U.S.[9] ZARXIO gross sales have been exceeding NEUPOGEN since Q3 2018 and combined ZARXIO and GRANIX gross sales exceeded NEUPOGEN gross sales since mid-2017.[10]

[7] Amgen data on file. Methodology: Calculation of unit share is based on units sold for the following products in the short acting GCSF market basket: NEUPOGEN, ZARXIO, GRANIX, NIVESTYM, and LEUKINE. The analysis is based on IQVIA DDD data, supplemented with Amgen proprietary data and estimates for select customer segments not included in IMS DDD. Because IQVIA DDD is not 100 percent complete, Amgen uses proprietary data and estimates to fill gaps.
[8] Ibid.
[9] Amgen data on file. Methodology: Calculation of share by gross sales is based on units sold times WAC for the following products in the short acting GCSF market basket: NEUPOGEN, ZARXIO, GRANIX, NIVESTYM, and LEUKINE. The analysis is based on IQVIA DDD data, supplemented with Amgen proprietary data and estimates for select customer segments not included in IMS DDD. Because IQVIA DDD is not 100 percent complete, Amgen uses proprietary data and estimates to fill gaps.
[10] Ibid.

3. You stated in the hearing you did not know the price of Neupogen in Denmark. Now that you are able to determine it, what is the price of Neupogen in Denmark today? If it is lower than Neupogen's price in the United States, does that support your contention that biosimilar competition is working in the Neupogen market? Also, can you please report how much more money patients and payers in the United States, including the Medicare program, have spent on Neupogen relative to what they would have paid had Neupogen sold for the price it had in Denmark during the same time period?

We respectfully disagree with your assertion that Denmark does not have government price controls. The Danish healthcare system differs from the U.S. system in significant ways. Denmark is a single payer system with price controls, such as the imposition of price caps for medicines and a national formulary, that result in restricted access to drugs.[11] An analysis looking at the availability of new cancer drugs between 2011 and 2018 demonstrates that access is more constrained in Denmark compared to the U.S. While 96 percent of new cancer drugs were available in the U.S., only 66 percent of new cancer medicines were available to patients in Denmark.[12] Denmark also currently utilizes national tenders with approximately 80 percent of volume adjudicated to the winner.[13] Further, biosimilars have been available in Denmark for a decade, since 2009. The current list price of a NEUPOGEN injection in Denmark is between US$84 and US$142 depending on presentation and dose, but that is not a like-to-like comparison to U.S. pricing given the tender dynamics and price controls in the Danish healthcare system.

Comparing the Denmark price for NEUPOGEN to the U.S. price is not the best metric to assess the performance of the U.S. biosimilar market given that Denmark uses a government-imposed pricing system while the U.S. uses a free market system that produces better access for patients. A better metric is to look at the effect of biosimilars in the U.S. market. As noted above, as of July 2019 the unit sales share of NEUPOGEN in the U.S. is 32 percent compared to biosimilar and biologic competitors which have more than double the short acting GCSF unit sales.[14] ZARXIO (a biosimilar) has Medicare reimbursement rates that are 38 percent below the reference product.[15] These data illustrate the impact that biosimilars are already having in the U.S. healthcare marketplace, promoting increased competition and cost savings to patients and payers as intended.

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[11] Badger, D. Examination of International Drug Pricing Policies in Selected Countries Shows Prevalent Government Control over Pricing and Restrictions on Access, p.11-12 (March 2019). Available at https://galen.org/assets/Badger-Report-March-2019.pdf.

[12] PhRMA Analysis of IQVIA Analytics Link and Food and Drug Administration/European Medicines Agency and PMDA Data (Nov. 2018). Available at http://phrma-docs.phrma.org/files/dmfile/IPI-Model---Comparison-of-Cancer-Medicine-Availability---012819.pdf.

[13] Background Note for the G-CSF Therapy Area, RADS (Rådet for Anvendelse af Dyr Sygehusmedicin), p. 22 (October 2014). Available at https://rads.dk/media/2548/baggrundsnotat-for-terapiomraadet-for-g-csf.pdf.

[14] Amgen data on file. Methodology: Calculation of market share is based on units sold for the following products in the short acting GCSF market basket: NEUPOGEN, ZARXIO, GRANIX, NIVESTYM, and LEUKINE. The analysis is based on IQVIA DDD data, supplemented with Amgen proprietary data and estimates for select customer segments not included in IMS DDD. Because IQVIA DDD is not 100 percent complete, Amgen uses proprietary data and estimates to fill gaps.

[15] CMS 2019 ASP Drug Pricing Files. Available at https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2019ASPFiles.html.

In the U.S., biosimilars still are a new market, but growing rapidly with nine biosimilars currently on the market (six launched in the last year alone) competing against six separate originator medicines. The scientifically sound regulatory pathway in the U.S. has produced 23 biosimilar approvals as of July 2019.[16] In addition, the FDA's Biosimilar Development Program encompasses 77 manufacturer development programs as March 2019.[17] Biosimilars are on track to introduce competition in the U.S. that is projected to save billions. A recent analysis by IQVIA projects that biosimilars will save nearly $160 billion in the U.S. between 2019 and 2023.[18]

We are not able to report how much more payers and patients in the U.S. have spent on NEUPOGEN relative to what would have been spent if we sold the product at the Denmark price because it is not possible for us to calculate this accurately. For example, we do not know how much commercial payers in the U.S. paid for NEUPOGEN because ultimately that depends on the contractually agreed upon rate between each payer and each provider they contract with (e.g. physicians or physician groups, hospitals, and pharmacies). These contracts are not available to us. We also do not know what the patient cost is for the product because the patient out-of-pocket cost will depend on a patient's specific benefit plan design, as well as the availability of secondary insurance. Even if we had sufficient data to do this type of analysis, it would not be an apples-to-apples comparison given that it would be comparing a government-run healthcare system with price controls and access restrictions (Denmark) to a free market system (the U.S.).

The Honorable Michael C. Burgess, M.D.

1. Mr. Niksefat, you mentioned in your testimony that Amgen lowered the list price of Repatha by 60 percent last year, but that patients have largely not seen the benefit of this lower list price. At the end of the day, we should be working to lower out-of-pocket costs for patients, and Amgen's attempt to do so is not playing out as anticipated. Is there any action that Congress or the Department of Health and Human Services should consider to alter the incentive structure surrounding list prices, or is this something that the market can sort out on its own?

As discussed in my testimony, we believe there are a number of actions Congress or the Department of Health and Human Services could take to lower-out-of-pocket costs for patients and provide incentives to lower list prices. Below I briefly summarize two recommendations:

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[16] FDA Biosimilar Product Information (updated July 23, 2019). Available at https://www.fda.gov/drugs/biosimilars/biosimilar-product-information.
[17] FDA-TRACK: Center for Drug Evaluation & Research - Pre-Approval Safety Review - Biosimilars Dashboard (updated March 31, 2019). Available at https://www.fda.gov/about-fda/fda-track-agency-wide-program-performance/fda-track-center-drug-evaluation-research-pre-approval-safety-review-biosimilars-dashboard.
[18] The Global Use of Medicine in 2019 and Outlook to 2023, IQVIA, p.21 (January 2019). Available at https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/the-global-use-of-medicine-in-2019-and-outlook-to-2023.pdf.

- **CMS Guidance to Part D Plans Addressing List Price Reductions:** CMS can take immediate action by issuing guidance highlighting that, in instances where manufacturers lower list price for medicines that puts them below the specialty tier threshold of $670, plans should move the lower list price drug from the specialty tier to a tier with better (or no worse) cost sharing (e.g., preferred brand). We hope to work with the Committee on this specific policy solution since it is a way to quickly reduce out-of-pocket costs for patients taking Repatha® (evolocumab). If CMS is unwilling to issue mid-year guidance, then the Committee could introduce legislation requiring CMS to make this change given that it would help patients access medicines at more affordable cost-sharing when manufacturers reduce list prices.

- **Require Rebates to Be Passed on to Patients at the Pharmacy Counter:** We are supportive of policy changes that would ensure savings from rebates flow directly to patients. Even in the face of net price declines as we experienced last year, patients are not seeing the benefits of these declines. At both the state and federal level, we are supportive of lawmakers' efforts to look for ways to ensure patients can access these rebate dollars to improve affordability for patients.

2. Something I find particularly concerning about our drug supply chain is the possibility of drug shortages. These can occur because of natural disasters, manufacturing issues, or business decisions. What are each of your respective companies doing to prevent drug shortages?

With nearly four decades of experience in biotechnology and a record of reliably supplying medicines to patients, Amgen is known worldwide as a leader in research, development, and manufacturing of complex biologic therapies. Amgen has strong track record of reliable supply. According to ongoing data monitoring of drug shortages by the American Society of Health System Pharmacists dating back to 2007, Amgen had zero drug shortages.[19]

Drug shortages can have a significant impact on patients and healthcare providers. As identified by the U.S. Food and Drug Administration, quality, manufacturing, and capacity issues are major reasons for many of these drug shortages.

We are deeply committed to ensuring doctors and patients can rely on the quality and availability of our treatments. The Amgen approach to providing a continuous supply of biologic therapies has four key elements:

- PREVENTION which includes promoting exemplary regulatory compliance, robust quality management processes, operational excellence, supply chain security, infrastructure investments, and business continuity planning;

[19] Amgen's 2018 Biosimilars Trends Report. p. 4. Available at https://www.amgenbiosimilars.com/pdfs/2018_trends_report.pdf.

- TECHNOLOGY to enhance product purity and the robustness of the manufacturing process;

- INVENTORY MANAGEMENT to help us have the right quantities of the product housed in diverse geographic locations; and

- REDUNDANT MANUFACTURING capacity in multiple geographic locations and back-up suppliers for raw materials.

Beyond complying with current good manufacturing practices (cGMP) and implementing a robust quality management system, Amgen takes extra steps to help ensure a reliable supply to every patient, every time. As a first step, Amgen invests in inventory management at multiple points in the supply chain to mitigate potential risks of disruptions to supply (e.g., natural disasters).

Additionally, Amgen maintains appropriate levels of raw materials by diversifying suppliers of sourced raw materials and storing high-risk raw materials in multiple geographical locations to safeguard their availability. By managing relationships with suppliers so that raw materials requirements are understood and shared between both parties, Amgen is able to source high-quality raw materials to minimize reprocessing and potential product manufacturing issues, and to help facilitate consistent product quality.

Maintaining diverse manufacturing capabilities requires significant investment in internal manufacturing and contract manufacturing capabilities. Amgen has invested more than $1.6 billion in supply management since 2005. By maintaining a network of plants across seven Amgen manufacturing sites (diversification), supplemented with additional capacity at contract manufacturers, Amgen is able to implement back-up manufacturing capabilities when needed. Amgen is also able to actively manage robust and secure distribution networks, by establishing well-controlled temperature ("cold chain") distribution channels to maintain the quality of each product and utilize multiple approaches to mitigate distribution-related security risks to supply. These include controlled shipping lanes using temperature-validated shipping containers to maintain chain of custody, anti-theft and anti-counterfeiting measures to mitigate the risk of diversion and adulteration, and risk management programs to systematically address risks as they develop.

3. Do you have processes in place to minimize the negative effects of drug shortages should one of your manufacturing facilities offline?

Amgen's significant investments in promoting reliable supply were tested in 2017 when Hurricane Maria hit Puerto Rico, where Amgen's largest manufacturing site is located. In the aftermath of the storm, Amgen provided support to our staff members and the local community while implementing our robust business continuity plans and restoring manufacturing operations at our site in Juncos. The company continued to provide an uninterrupted supply of medicines for patients around the world by:

- Maintaining inventory levels to address unplanned situations:
    - Shortly after the storm, our warehouse in Puerto Rico resumed shipments of medicines from inventory maintained in a temperature-controlled bunker.
    - The majority of our finished goods inventory is maintained on the U.S. mainland.

- Investing in capacity and redundant facilities:
    - Amgen's global manufacturing network includes a redundant fill/finish facility in Ireland and we have relationships with established contract manufacturers in the U.S. and Europe for additional capacity.
    - We activated manufacturing and packaging lines at our own sites in Ireland and the Netherlands and at contract manufacturers in the U.S. and Europe to absorb some production volume and serve as a relief valve while our Puerto Rico site resumed full operations.

- Exercising our business continuity plans on a regular basis:
    - Following its established plans, the Puerto Rico site was prepared and responded before, during, and after the hurricane.
        - Amgen has a network of back-up generators which powered the site and regular deliveries of diesel fuel were supplied under pre-arranged contracts.
        - When municipal water service was interrupted, Amgen used on-site wells and water storage tanks.
        - Supplies of medical-grade oxygen and nitrogen on the island were limited. Amgen arranged deliveries via ship of both types of gas from the U.S. mainland and other countries, and established alternate supply chains until reliable service on the island was restored.

    - A cross-functional team from across the company supported the site recovery efforts with materials/supplies, logistics and engineering support, and resources for staff and the local community.

For more details on Amgen's response following Hurricane Maria, please see this video: https://youtu.be/h5AXDsQNX3A

The Honorable John Shimkus

1. Given that most of the witnesses on the panel have referenced the role of creating value in the health care supply chain, please comment on: Existing areas where Congress or the Administration may have needlessly added to the cost that patients or the government pays for a particular product, service, or intervention. For example, do you have recommendations on how reforms to existing laws like Stark and the Anti-Kickback Statute could accelerate value-based contracting within Medicare and Medicare Advantage?

Amgen has strong interest in entering into additional value-based contracting arrangements. However regulatory barriers are preventing the ability to drive more innovative agreements. For example, if we enter into a value-based contract which results in a large payment because a patient did not achieve the expected clinical outcome, it could trigger Medicaid best price implications for our medicine in all 50 states. Similarly, we would like to see safe harbors created that would give the market confidence that these types of arrangements do not run afoul of the Anti-Kickback Statute. Therefore, we are supportive of regulatory or legislative approaches that would exempt value-based arrangements from Medicaid "best price" while at the same time creating a new Anti-Kickback Statute "safe harbor." These recommendations are consistent with the positions of a number of trade groups and coalitions, such as PhRMA and the Health Leadership Council.[20]

Amgen believes this could be done in a manner that requires such arrangements to entail some portion of risk assumed by both parties to the agreement to qualify for such exemptions. These changes would improve the ability of manufacturers to enter into more innovative value-based agreements with payers in a meaningful way, which in turn could yield savings and better deliver downstream quality of care.

2. How do we ensure that these value-based reforms benefit patients and protect taxpayers?

We agree with CMS that value-based reforms support the "three-part aim" of: 1) better care for individuals; 2) better health for populations; and 3) lower costs. We believe that robust market-based negotiations between payers and manufacturers will result in arrangements that enhance quality of care and reduce costs for patients, payors, and plans. That is why we support removal of outdated regulatory barriers that impede these arrangements.

To the extent that legislative changes allow greater flexibility for manufacturers to enter into value-based agreements with Medicare - this could enhance quality and would likely produce savings for the Medicare program, taxpayers, and beneficiaries.

[20] See PhRMA and HLC comment letters on OIG–0803–N Request for Information Regarding the Anti-Kickback Statute and Beneficiary Inducements CMP available at https://www.regulations.gov/document?D=HHSIG-2018-0002-0317 and https://www.hlc.org/app/uploads/download.php?dl=app/uploads/2017/02/HLC-Comment-Letter-OIG-AKS_FINAL.pdf and PhRMA comments on HHS Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs available at https://www.regulations.gov/document?D=CMS-2018-0075-2808.