Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA. 91320
www.amgen.com

TESTIMONY OF ROBERT A. BRADWAY
CHAIRMAN AND CHIEF EXECUTIVE OFFICER
AMGEN INC.
BEFORE THE U.S. HOUSE COMMITTEE ON OVERSIGHT AND REFORM
October 1, 2020

Full Committee Chairwoman Maloney, Ranking Member Comer and Members of the Committee, I am Robert A. Bradway, Chairman and Chief Executive Officer of Amgen Inc. I appreciate the opportunity to provide written testimony about how best to ensure that innovative, life-changing medicines from Amgen and others are accessible and affordable to the many patients who need them.

We have entered a golden age of innovation where remarkable advances in science and technology are giving us powerful new weapons in the fight against COVID-19 and some of the most serious diseases we face as a society. We have made considerable investments researching possible treatments for COVID-19, including a recent collaboration with Eli Lilly and Company to manufacture a promising antibody therapy, and look forward to working with the government, academia and industry to bring meaningful treatments to patients. Separate from COVID-19, we continue to race to bring helpful treatments to patients with serious conditions including cancer, heart disease, and inflammatory conditions such as asthma.

In recent years, however, after obtaining Food and Drug Administration (FDA) approval, we have found that the real challenge is overcoming barriers that keep medicines out of reach for those who need them. First, there are prior authorization barriers imposed by payers that restrict access by burdening physicians with various steps to obtain approval for their patients to access the medicine the physician determined is medically necessary. Then there are barriers at the pharmacy counter when people find out what they have to pay out of pocket for the medicine they need. This, in turn, is a function of a dizzying array of variables such as the design of insurance plans, current deductible status, and other factors making it hard to know in advance how much a given prescription will cost.

I commend the Committee for holding this hearing to better understand how this complex drug pricing system works in the U.S. marketplace. We have been cooperating with the Committee's request for pricing information and I appreciate the opportunity to provide Amgen's perspective.

Amgen was founded 40 years ago by biotech entrepreneurs who set up shop in a small office park in Thousand Oaks, California. Today, Amgen is still based in Thousand Oaks, but we now employ approximately 23,000 people, including nearly 14,000 in the U.S. We also operate one of the most reliable biologics manufacturing networks in the world, including facilities in California, Massachusetts, Rhode Island, Puerto Rico and Kentucky and we are continuing to invest in the U.S. by building a new, eco-friendly manufacturing plant in Rhode Island next to our existing facility there.

Our first medicine, Epogen®, was approved by the U.S. Food and Drug Administration in 1989 and has been prescribed to approximately 2.8 million patients on dialysis.[i] Our portfolio now includes 23 medicines that treat many of the world's most devastating and costly illnesses, including cancer, cardiovascular disease, migraine, and osteoporosis.

We are committed to the discovery and development of new medicines and to this end, we invested $4 billion in research and development (R&D) just last year and nearly $19 billion over the last five years. Today, more than 33,000 patients globally are enrolled in over 150 clinical trials for new Amgen medicines.[ii] We are also engaged in the fight to understand, treat, and prevent COVID-19, including taking the following steps:

- Entering into a manufacturing collaboration with Eli Lilly for antibody therapies for the prevention and/or treatment of COVID-19;
- Investigating use of Otezla® as a potential immuno-modulatory treatment in adult patients with COVID-19 through several clinical studies;
- Researching what might prove to be the second generation of neutralizing antibody therapies based on characteristics of antibodies produced by patients who had COVID-19 but who did not suffer symptoms;
- Studying the genetics and epidemiology of the disease to better understand how the virus spreads and mutates; and
- Partnering with the National Institutes of Health (NIH) through the Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV) – a public/private collaboration to accelerate COVID-19 treatments and vaccines.

Additionally, Amgen has invested over $2 billion in recent years to build an industry-leading biosimilars business – with a portfolio of ten biosimilars, including four that are FDA-approved. Backed by Amgen's four decades of biologics expertise, our high-quality biosimilars can potentially offer more affordable, life-altering treatment options that contribute to the sustainability of our healthcare system and allow for greater investment in new medicines for patients.[iii]

Tremendous advances in science and technology have put us on the cusp of what we believe will come to be seen as the "biocentury." Just as physics and engineering led to extraordinary advances in the 20th century, we are now at a true inflection point in terms of our understanding of biology and, with it, our ability to take on serious illness, such as cancer and cardiovascular disease, and help people live longer, healthier lives. The promise of the biocentury comes at a critical juncture for our country, as an estimated 10,000 Americans will turn 65 every day for the next 20 years – leading to an inexorable rise in diseases associated with the aging process.[iv]

Today, the biopharmaceutical industry discovers more innovative medicines in the U.S. than anywhere else in the world and our market-based system ensures that Americans get broader and faster access to these medicines than patients in other countries. Prescription medicines play a crucial role in improving health outcomes and reduce overall health care costs. Better use of medicines, such as improved adherence to needed treatments, offers the opportunity for better results for patients and an estimated $213 billion per year in health care savings.[v]

Despite these potential savings, much of the public debate about the cost of medicines has unhelpfully focused on list prices. Pharmaceutical companies set the Wholesale Acquisition Cost (known

as "WAC") which is often referred to as the "list price." While the WAC or list price for each of Amgen's products is in part anchored to a medicine's value driven price – the value a medicine is likely to deliver to patients, to payers, and to society – the price is frequently established against a competitive backdrop. List price is the price we charge to wholesalers and distributors who purchase our medicines, but it does not reflect the true price of the medicine after the rebates and discounts we negotiate with the complex web of wholesalers, distributors, hospitals, providers, pharmacies, pharmacy benefit managers (PBMs), health plans and other entities in the supply chain. In the current health care system, competition is driving ever-larger rebates on medicines, with net prices for brand-name medicines in the U.S. increasing less than the overall rate of inflation in 2018.[vi]

So why are we seeing that too many patients are increasingly having difficulty affording their prescription medicines? One reason is that unlike any other category of healthcare, list price serves as a primary basis of determining patient out-of-pocket costs for prescription medicines. As a result, the negotiated savings of the market-based healthcare system do not reach patients at the pharmacy counter, especially as co-payments and deductibles on medicines have increased and as high-deductible health plans become more prevalent. The problem is not that the market-based negotiations are not effective at generating savings, it is that the savings never make their way to patients in the form of reduced out-of-pocket costs.

We want to continue working with Congress to advance solutions to lower out-of-pocket costs for patients. But there is too often a singular and overly simplistic focus on the list price of medicines and pharmaceutical companies' role in drug pricing. The truth is that without others in the healthcare system – such as insurance companies, PBMs, employers, drug distributors, hospitals, and physicians – working together with pharmaceutical companies toward solutions, we will make little progress for patients.

In this testimony, I will first describe some of the actions Amgen is taking to address the affordability challenges that face our patients. We take seriously our duty to price products responsibly and have put forward several solutions to health plans, PBMs and patients that lower the net price of many Amgen medicines.

Second, I will share some perspective on Enbrel® and Sensipar® -- Amgen medicines that are of particular interest to the Committee.

Third, I will review some of the policy solutions that Amgen supports to improve access and affordability for our patients.

Part 1: Amgen Actions to Address Patient Affordability Challenges

In the U.S., people know intuitively that the healthcare system is cumbersome and the upward curve of cost is not sustainable. At Amgen, we are sensitive to this reality and have taken a number of steps to proactively offer solutions to address affordability issues for our patients. Since 2018, the average net price for Amgen medicines has declined, and we expect a continued mid-single digit percentage decline in the net price across our U.S. portfolio of products in 2020 due to rebates and

discounts negotiated with payers, providers and others in the drug distribution chain to ensure patients continue to have access to our medicines. The average list price increase across Amgen's entire U.S. portfolio of products is in line with inflation and key pricing indices. And to repeat, our net prices have declined.

Because of the way the U.S. healthcare system is organized, we recognize that many uninsured and vulnerable patients need extra help affording their medicines. For that reason, we established the Amgen Safety Net Foundation to provide access to our medicines at no cost to qualifying patients in the U.S. (including Puerto Rico) who have a financial need and are uninsured or have an insurance plan that excludes the prescribed Amgen medicine. Since 2008, the Amgen Safety Net Foundation has provided $7 billion in free medicines to assist these U.S. patients. In addition, Amgen offers generous copay assistance to reduce out-of-pocket costs for commercially insured individuals regardless of income.

Beyond lowering our net prices and providing assistance to qualifying patients, Amgen has taken a number of concrete and innovative steps in recent years to ensure the affordability of our medicines in order to ensure patients ultimately receive the benefit as reflected in their out of pocket costs. I would like to highlight two Amgen medicines and other examples that illustrate our commitment to addressing affordability for our patients.

List Price Reduction for Repatha®

Repatha®, a PCSK9 inhibitor, is an Amgen medicine proven to reduce heart attacks and stroke in patients with cardiovascular disease and persistently high cholesterol levels. Barriers to Repatha®, put in place by insurance companies and PBMs, were preventing clinically appropriate patients from getting the drug. As a result, nearly 75% of Medicare patients prescribed a PCSK9 were not able to fill their prescriptions. And this was after prescribing doctors' staff spent countless hours filling out lengthy forms and fighting to gain access to Repatha®, a medicine for which many patients have no alternative therapy to mitigate their risk.

In 2018, Amgen took the unprecedented step of making Repatha® available at a 60% reduced list price to help lower patients' out-of-pocket costs. We estimate that more than half of all potential Repatha® patients are Medicare beneficiaries. For Medicare patients in particular, the lower list price should have immediately reduced patient out-of-pocket costs from approximately $280 - $370 per month on a specialty cost sharing tier to $25 - $50 per month on a preferred brand cost sharing tier. However, after our list price reduction for Repatha®, it took the Part D plans more than a year to pass these savings on to Medicare patients so that they could access Repatha®.

For this medicine, we saw a particularly vexing problem and we acted to address it. This is indicative of a market in need of reform and Amgen supports policy changes that would ensure that savings from rebates flow directly to patients. We are encouraged by the Administration's recent proposal to help reform this broken rebate system and we welcome additional reforms that put patients first and preserve incentives for companies like Amgen to innovate on their behalf.

Leveraging 21st Century CURES to Establish a Lower than Expected List Price for Aimovig®

In 2018, after many years of research and development, we launched Aimovig®, a novel treatment developed specifically for migraine prevention and the first FDA-approved treatment to block the calcitonin gene-related peptide receptor (CGRP-R). For patients with migraine, no new preventive options had been available for many years and significant unmet need remains for these patients. Migraine is ranked among the top 10 causes of years-lived-with-disability worldwide.[vii] The economic impact is profound, with ~$20 billion in direct and indirect costs attributable to migraine in the U.S. alone.[viii]

Prior to approval, Amgen was able to use key new communication pathways provided by the 21st Century CURES Act and subsequent FDA guidance to have economic discussions with payers around this important innovation. This dialogue was a key factor in our decision to introduce Aimovig® at a list price that was approximately 20% to 65% below initial market expectations.[ix] More than 440,000 patients worldwide have been prescribed Aimovig® since its approval, with over 1 million prescriptions filled.[x]

Within a few months of Aimovig®'s launch, two competitors entered the migraine market, which has driven the net price of our product down further. While this demonstrates that market-based competition is working to reduce costs in the system and manufacturers are offering lower net prices, most of today's migraine sufferers are not directly benefiting from negotiated discounts at the pharmacy counter. As I will articulate below, Amgen believes that there are policy solutions to ensure patients get access to the lower prices that are negotiated on the product they need and that they see this benefit in the form of lower out-of-pocket costs at the pharmacy counter.

Developing a Robust Portfolio of Biosimilars

Although Amgen is known primarily as a biologics innovator, when Congress enacted the Biologics Price Competition and Innovation Act (BPCIA), which created the biosimilars approval pathway, we recognized that biosimilars would become an important part of broadening patient and physician options. We realized that our expertise in developing and manufacturing biologics also would apply to biosimilars and consequently committed billions to build an industry-leading biosimilars business. We launched our first two biosimilars in the U.S. last year to compete with two of the top-selling cancer medicines in the country. We priced both biosimilars at a 15% discount to the originator products, creating the opportunity for immediate and significant savings for patients. And we have recently launched our third biosimilar in the U.S.

As competition has grown, lower prices have followed. Medicare and commercial payers are seeing prices decline for both originator and biosimilar medicines in marketplaces where biosimilar competition has begun.

For example, as an originator product manufacturer, we've witnessed the impact of biosimilar competition on several originator biologics. Take the oncology supportive care market: filgrastim biosimilars have experienced strong adoption, and our share, as the innovator of this biologic, has dropped by roughly 70 percent.[xi] As the oldest biosimilar class in the U.S., this progress bodes well for newer products.

The biosimilar marketplace is now flourishing in the U.S. and functioning as we hope free markets would. The remarkable 143 percent increase in launched biosimilars in the past year reinforces that perspective. Every company finds itself winning and losing some market share, hallmarks of a competitive marketplace.

It's clear that competition is robust, biosimilar market share is increasing, prices are coming down, and substantial savings are being generated. According to an IQVIA report, projected cost savings in the next 5 to 10 years of approximately $150 billion are expected from biosimilar competition in the U.S.[xii] In 2020, we can say with confidence that biosimilars can help deliver a brighter future for our healthcare system.

We plan to launch several additional biosimilars in the coming years and continue to believe that they will bring meaningful cost savings to patients and to the healthcare system.

A Leader in Value-Based Partnerships and Value-Based Contracts

We're helping to evolve the complex health ecosystem by actively engaging with and leveraging the strengths of governments, manufacturers, academics, payers, and practitioners to enable health systems to co-create novel solutions to transform reactive care to more proactive, predictive and preventive care.

Amgen is engaged in over 160+ value-based partnerships, spanning all of our therapeutic areas of focus.[xiii] By engaging in value-based partnerships with entities across the healthcare system, Amgen hopes to develop mutually beneficial opportunities to reduce costs, improve care and enhance patient experiences. This reflects the company's belief that managing disease through innovative medicine is key to containing healthcare costs and improving population health.

In addition to our value-based partnerships, we are working with payers, PBMs, health plans, and other stakeholders to find new, innovative ways to work together to improve patient access to medicines while providing budget predictability that will help patients access the medicines they need. These include value-based contracts like that with Harvard Pilgrim Health Care in which we provide a rebate for the cost of Repatha® if a patient experiences a heart attack or stroke while on the drug. Separately, Oklahoma Health Care Authority and Amgen entered into a public-private contract for Enbrel® in 2020. This is the first value-based contract Amgen has in the Medicaid channel stipulating additional supplemental rebates paid contingent on real-world outcomes.

We believe outcomes-based contracts provide a valuable option to payers interested in evolving from volume-based contracts to those focused on the value medicines can bring to patients. Amgen has more than 120+ value-based contracts globally; 30 which are in the U.S.[xiv]

Part 2: Enbrel® and Sensipar® – Addressing Patient Needs and Providing Economic Value

ENBREL®

Enbrel® is an Amgen medicine that treats several autoimmune disorders that can have a devastating impact on patients, including those suffering from moderate-to-severe rheumatoid arthritis

(RA) and moderate-to-severe plaque psoriasis. Patients with these conditions have overactive immune systems that can cause severe inflammation. This inflammation is what causes severe joint damage, swelling, pain, and fatigue in patients with rheumatoid arthritis, and itchy and often painful raised patches of dead skin cells or scales in patients with plaque psoriasis. Enbrel® helps reduce joint pain and stiffness in patients with moderate to severe rheumatoid arthritis and juvenile idiopathic arthritis. In patients with psoriatic arthritis, Enbrel® helps reduce joint pain and stiffness, and improves skin symptoms. It also helps stop further joint damage, improves physical function and daily activities in patients with moderate to severe rheumatoid arthritis and psoriatic arthritis. For patients with moderate to severe plaque psoriasis, Enbrel® has been shown to help achieve clearer skin. The evidence base for Enbrel® has evolved dramatically over the years with multiple new indications and, importantly, provides demonstrated disease modification in addition to relief of signs and symptoms of disease.

Physicians who treat patients with autoimmune disorders like moderate to severe rheumatoid arthritis remind us that their waiting rooms used to be cluttered with canes, crutches, and wheelchairs – even stretchers. That's how debilitating untreated moderate-to-severe rheumatoid arthritis can be. That is no longer the case due to the introduction of innovative medicines like Enbrel®.

Along the way, Enbrel® has become one of the most studied biologic medicines.[xv] Enbrel®'s strong evidence base, costing hundreds of millions of dollars, includes large clinical registries and more than 100 trials globally involving approximately 115,000 patients.[xvi] In the U.S., over 29 million prescriptions have been dispensed across all indications since Enbrel® was approved.[xvii] Amgen also invested more than $1.6 billion in building and improving our manufacturing facilities so that we can produce sufficient quantities of products including Enbrel® to meet patient demand.

The list pricing of Enbrel®, often viewed as the "sticker price" of a medicine, has increased over the years as we have invested capital studying it for additional indications and introduced new, more patient-friendly formulations and administration methods. As an example, we recently introduced an easy-to-use, self-injection device specifically designed to meet the needs of moderate-to-severe rheumatoid arthritis patients and psoriatic arthritis patients.

But the primary reason the list price of Enbrel® has increased as much as it has is because the market for innovative products is structured in a way to benefit intermediaries and not in a way to get lower prices to patients. Enbrel® is in a highly competitive marketplace that includes approximately 20 other medications that are competing for formulary position with PBMs to enable patient access, including the largest pharmaceutical product in the world Humira®. In these highly competitive marketplaces, companies are forced to simultaneously compete both on lowest net price ("all in" price to the PBM) and highest total rebate. In a competitive market, we often have to pay higher and higher rebates to remain on formulary—even as list prices rise and the net price to the PBM often decreases. Because of the way PBMs structure these contracts, increases in list prices generally have limited impact on net prices but significantly increase total rebates paid to the PBMs. In light of this environment, Amgen has increased list prices over the years in response to competitor list price increases to remain available as a choice on PBM formularies. If we had not done so, we believe the PBMs would have simply removed Enbrel® from their formularies in favor of a competitor who provided a higher rebate to

the PBM. Since Enbrel® and its competitor products do not provide the same response in all patients, they are not simply interchangeable. If taken off formulary, many Enbrel® patients would not have access to the medicine that they and their doctor had determined worked best for them.

Unfortunately, the current rebate system in the U.S.—in which companies like Amgen pay billions of dollars in rebates to insurers and PBMs based on the list price of our medicines—creates a situation in which not getting kicked off formulary often requires counterintuitive pricing behavior. For example, PBMs can receive lower net prices but consumers instead see prices go up and see little relief at the pharmacy counter since these savings from the PBMs are often not passed on.

We do not like a system where we lower the net price of a drug yet our patients pay more, and we are advocating to change it. But it's the system that exists today and we must operate within it to stay competitive and ensure that patients have access to Enbrel®.

We strive to ensure that every patient who needs our medicine can get access to it. We understand that the dynamics that exist in today's supply chain, such as high coinsurance and deductible levels, can make needed therapies expensive for patients. This is why we sponsor industry leading patient support programs that provide medicine for free to those who cannot afford their medicine. As indicated above, we have provided $7 billion in medicines since 2008 under these programs.

SENSIPAR®

Sensipar® is an advanced therapy for secondary hyperparathyroidism in patients with chronic kidney disease on dialysis.

Before Sensipar® was approved in 2004, many patients were undertreated with older vitamin D therapies, eventually leaving many in need of having parathyroidectomy, a surgical procedure associated with distinct risks leading to potentially more complex disease management and high costs. Since the introduction of Sensipar®, the proportion of patients achieving treatment guidelines has steadily improved.

The list price of Sensipar® increased over time, reflecting Amgen's approximately $500M investment in ongoing research and development in support of this product and other medicines to support critically ill end-stage renal disease patients.[xviii] In 2018, the last patent covering the active ingredient in Sensipar® expired, which has ultimately led to generic competition and, as publicly available pricing information shows, lower prices. In fact, generics now have an estimated 95% volume market share of the cinacalcet market.[xix]

PATENTS

There have been increasing questions about the role of intellectual property in ensuring sustainable access to medicines. We believe that intellectual property is essential to innovators, like Amgen, that are bringing forward new medicines for patients with serious illness. Medical innovation now enables us to live longer and better lives than ever before, bringing benefits to patients, healthcare systems, and society.

This innovation is the product of large-scale, long-term, and high-risk investments since as few as one in ten drugs that even gets to the point of entering a clinical trial are successful and the average

cost of developing such a drug is estimated to be $2.6 billion. Patents help inventors obtain return on their investments in research and development, which encourages future research and investment that makes further drug development sustainable. These incentives also allow for incremental innovation while not extending exclusivity in perpetuity.

There have also been concerns about patents being used for lifecycle management of products that are going off patent. The lifecycle management process at Amgen evaluates how we can continue to add value for patients by making improvements to our products or the patient experience. This includes developing new formulations, new uses, new processes and new devices. Amgen works on these improvements "at risk," that is without knowing if the investment in the hoped-for results will pay off by benefitting patients. So in the cases in which Amgen does provide benefits to patients, we believe those improvements deserve patent protection.

In summary, biopharmaceutical research is an incremental process driven by the science, and ongoing innovation after product approval can lead to meaningful medical advances and improving the patient experience. We believe that protecting intellectual property is critical to fully develop a medicine's therapeutic potential for patients.

Part 3: Policy Solutions to Improve Affordability for Patients

We are focused on developing market driven policy solutions that improve affordability for our patients. For example, the benefit design of Medicare Part D creates affordability challenges in the initial coverage phase, coverage gap and the catastrophic levels of the benefit. Patients need help with challenges presented by an outdated benefit design in Part D so we look forward to working with Congress and the Administration on policy solutions designed to lower patient out of pocket costs at the pharmacy counter. More specifically, we are supportive of the following policy solutions to improve affordability for patients:

- **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. One approach would require that a portion of the rebate be passed through to patients at the pharmacy counter. We also support efforts to consider the Administration's recent Executive Order to reform how rebates are handled in the marketplace by moving from backend rebates to up front discounts in order to lower out-of-pocket costs for patients at the pharmacy counter. Without these changes, even in the face of net price declines, patients will not get the benefits of these declines. At the state level in 2019, five states considered requiring health plans to pass through at least a majority of rebates to patients; and last year, Louisiana became the first state requiring health plans to disclose to its insurance commissioner the percentage of rebates made available to enrollees at the pharmacy counter. 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. We strongly support these efforts and hope to continue to engage with the Administration and Congress on this topic going forward.

Rebates continue to be the single largest economic driver in the drug supply chain. At Amgen, we continue to try to lead on these issues. For example, as a large employer, our benefits structure with a large PBM is set up such that if our employees are faced with paying the list price of a covered prescription at the pharmacy counter, the discounts are passed through to them at the point of sale.

- **Embrace a Robust and Competitive Level Playing Field Between Innovators and Biosimilar Manufacturers:** When the BPCIA was enacted, creating the biosimilars approval pathway, we decided to invest in manufacturing high-quality, reliably supplied biosimilars. We believe the continued success and long-term viability of this market depends on a level playing field for competition and scientifically accurate information that establishes the confidence of patients, physicians, pharmacists, and payers – all of which are essential to achieving meaningful cost savings and multiple public health benefits.

  With this in mind, Congress should not adopt policies that provide for preferential reimbursement of a biosimilar over innovator medicines —- especially those that actually result in the cost of the biosimilar being greater to patients and the government than the cost of the innovator product.

  As a manufacturer of both innovator and biosimilar medicines, we do not believe biosimilars need special reimbursement advantages to successfully compete given that this new marketplace is already succeeding at driving savings to consumers. Furthermore, we believe such distortions would risk creating structural supply problems such as those experienced in the generic market.

  There have been some concerns raised that the biosimilar market is somehow "not working" or that we, in the U.S., are lagging behind Europe in this area. I would like to take this opportunity to correct these misperceptions based on our experiences from the U.S. marketplace.

  Our two currently marketed oncology biosimilars, which have a list price that is 15 percent lower than their originator biologic list price and a Medicare average sales price 20 percent lower than the originator biologics, are gaining adoption quickly, securing over 30 percent of their respective share in the U.S. in the last year. This is generating significant cost savings for both Medicare patients and commercial payers.

  Amgen has faced biosimilar market competition in the U.S. since 2015, and now faces competition from multiple biosimilars for three of our brand medicines. For example, biosimilars that compete against our originator product Neupogen® have achieved majority market share and meaningful cost reductions (e.g., short-acting granulocyte colony stimulating factor (GCSF) competitors have achieved more than 70 percent share in five years. Long-acting GCSF biosimilars have achieved 20 percent share in 12 months).[xx] By any metric, these examples reflect that the marketplace with biosimilar competition is an emerging success.

  With respect to comparisons to Europe, the U.S. is not behind. The European Union (EU) biosimilar pathway was established in 2005. During the first eight years of the EU pathway, five

biosimilars were approved. The U.S. biosimilar pathway was implemented in 2010. During the first ten years of the U.S. pathway, the FDA has approved 28 biosimilars, with 18 currently on the U.S. market.[xxi] This demonstrates the level of interest and commitment by manufacturers in the growth and development of the U.S. biosimilars market.

Biosimilars have an important place in the evolving U.S. market, and the competition promoted by biosimilars will result in cost savings that create budgetary space for new innovations that will also be valued in the healthcare system. Robust and fairly based biosimilar competition on a level playing field is the best way to achieve meaningful cost savings for the healthcare system, including patients, physicians, pharmacists, and payers, in a way that builds market stability that can be realized over the long term.

Conclusion

In closing, we believe that innovative biopharmaceuticals are part of the solution to the significant burden of serious diseases that impact patients and society. What we need is more innovation, not less. Changes are needed to encourage innovation while providing patients access to these innovative medicines.

As the examples of our own medicines discussed above show, we have implemented reforms to improve affordability for our patients. Whether we are dramatically cutting the list price of our medicines, as we did with Repatha®…or significantly increasing the rebates we pay for our medicines to lower the net price, as we've done with Enbrel®…too many patients still don't benefit.

However, this is not something that a single manufacturer or even an industry can make happen. Changing this system requires help from all stakeholders and Amgen stands ready to work with members of both parties and the Administration to develop policy solutions to help improve access and affordability for our patients.

There are so many more diseases to confront and patients to help. If we all stay focused on what's best for patients, I'm confident we will end up in a better place.

---

[i] Amgen data on file, 2020.

[ii] Amgen 2019 Annual Report & Shareholder Letter https://wwwext.amgen.com/media/featured-news/2020/03/2019-letter-to-shareholders/

[iii] IQVIA Report (2018). The Impact of Biosimilar Competition in Europe.

[iv] U.S. Census 2019. https://www.census.gov/library/stories/2019/12/by-2030-all-baby-boomers-will-be-age-65-or-older.html

[v] IMS Institute for Healthcare Informatics. Avoidable Costs in U.S. Healthcare: The $200 billion opportunity from using medicines more responsibly. June 2013.

[vi] IQVIA. The Global Use of Medicine in 2019 and Outlook to 2023. January 2019.

[vii] Goadsby et al. A Controlled Trial of Erenumab for Episodic Migraine. *N Engl J Med 2017*; 377:2123-2132.

[viii] Hawkins K, et al. Indirect cost burden of migraine in the United States. *J Occup Environ Med*. 2007 Apr;49(4):368-74. Hawkins et al. Direct Cost Burden Among Insured US Employees With Migraine. *Headache.* 2008;48:553-563.

[ix] Optum data. https://www.optum.com/resources/library/new-migraine-drugs.html

[x] Data on File. Novartis. Q2 2020 Financial Report. July 2020.

[xi] IQVIA Report 2020 - Q2'20 sales data through July 3, 2020; Monthly rollup based on 4-4-5 calendar.

[xii] IQVIA. The Global Use of Medicine in 2019 and Outlook to 2023. January 2019. Available at: https://www.iqvia.com/institute/reports/the-global-use-of-medicine-in-2019-and-outlook-to-2023.

[xiii] Amgen data on file.

[xiv] Amgen data on file.

[xv] Amgen data on file.

[xvi] Amgen data on file.

[xvii] Amgen data on file.

[xviii] Amgen data on file.

[xix] Amgen data on file.

[xx] Amgen data on file.

[xxi] U.S. Food and Drug Administration. FDA-Approved Biosimilar Products, Biosimilar Product Information. July 2020.

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
7500 Security Boulevard, Mail Stop 00-00-00
Baltimore, Maryland 21244-1850

Medicare Drug Rebate and Negotiations Group

Maximum Fair Price (MFP) Explanation for Enbrel

Introduction

In August 2022, President Biden signed the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169) into law. For the first time, the law provides Medicare with the ability to directly negotiate the prices of certain high expenditure, single source drugs without generic or biosimilar competition. On March 15, 2023, the Centers for Medicare & Medicaid Services (CMS) issued initial guidance for the Medicare Drug Price Negotiation Program (the "Negotiation Program"), including requests for public comment on key elements. On June 30, 2023, CMS issued revised guidance detailing the requirements and parameters of the Negotiation Program for the first cycle of negotiations.[1] CMS engaged in negotiations with participating manufacturers between October 1, 2023 and August 1, 2024. These negotiations resulted in agreements establishing prices (which the IRA refers to as "maximum fair prices" or "MFPs") that will be effective beginning in 2026 (the first cycle of negotiations is referred to as negotiations for "initial price applicability year 2026" because any agreed-upon prices will be effective in 2026). CMS published the agreed-upon MFPs on August 15, 2024.

The MFP explanation for Enbrel for the agreed-upon MFP that resulted from the negotiations for initial price applicability year 2026 with Immunex Corporation, the manufacturer of Enbrel (the "Primary Manufacturer"), provides information about the negotiations for Enbrel. This information includes CMS' perspective on the data considered that had the greatest impact in CMS' determination of offers and consideration of counteroffers during the negotiation process through which the parties reached agreement on an MFP.[2] In some respects, the Primary Manufacturer had a different perspective on the relevant data. The parties to the negotiation had productive exchanges during the negotiation meetings described below in which they discussed their respective views, and these exchanges resulted in the exchange of offer(s) and counteroffer(s) among the parties and, ultimately, an agreed-upon MFP for Enbrel.

On the basis of the factors described below and the related considerations and evidence, CMS negotiated with the Primary Manufacturer in good faith and consistent with the requirements of the law on behalf of people with Medicare and the Medicare program. Throughout the negotiation process and in accordance with the IRA, CMS' goal was to achieve agreement with the Primary Manufacturer on the lowest possible MFP for Enbrel that would be consistent with the process defined in the IRA for these price negotiations. CMS believes that the agreed-upon MFP achieves this aim. The negotiation process

[1] The Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191 – 1198 of the Social Security Act for Initial Price Applicability Year 2026, is referred to throughout this document as the revised guidance.

[2] Section 1195(a)(2) of the Social Security Act (the "Act") requires CMS to publish an explanation for the MFP with respect to the factors as applied under section 1194(e) for each selected drug. The MFP explanation is discussed in section 60.6.1 of the revised guidance.

ended in both parties agreeing to an MFP of $2,355.00 for Enbrel by the conclusion of the negotiation period on August 1, 2024.[3] The agreed-upon MFP is set to take effect on January 1, 2026.

The MFP explanation contains the following components:

- MFP Explanation Narrative for Enbrel
  - Summary of the Negotiation Process
  - Indications for Enbrel
  - Factors Applied
  - Manufacturer-Specific Data
  - Evidence about Enbrel and Therapeutic Alternatives to Enbrel
    - Therapeutic Alternatives
    - Outcomes and Additional Considerations
  - Citations to Data Reviewed during the Negotiation Process for Enbrel
- Redacted Negotiation Meeting Summaries for Enbrel
- Redacted Data Submitted by the Primary Manufacturer and Other Interested Parties for Enbrel

MFP Explanation Narrative for Enbrel

Summary of the Negotiation Process

CMS followed the negotiation process laid out in the IRA and in the revised guidance. On August 29, 2023, CMS announced the 10 selected drugs for the first cycle of negotiations, which included Enbrel. The Primary Manufacturers of the selected drugs signed agreements to participate in the Negotiation Program by the deadline in the IRA of October 1, 2023 and submitted information on the selected drugs by the deadline in the IRA of October 2, 2023.

CMS collected relevant data from numerous sources, such as written submissions from the Primary Manufacturers and other interested parties in response to an information collection request issued for the Negotiation Program (referred to as the "Negotiation Program information collection request" throughout this document), feedback from patient-focused listening sessions, meetings between CMS and the Primary Manufacturers to discuss the information submitted, and CMS' literature review.[4]

Using the information collected, CMS then developed initial offers for the selected drugs, which were based on the factors outlined in the IRA for CMS' determination of offers and which CMS developed in accordance with the process described in the revised guidance.[5] As required by the IRA, CMS' initial offers each included a concise justification on the range of evidence and other information within the negotiation factors that CMS found compelling during the development of the initial offer. The Primary Manufacturers each responded by declining CMS' initial offer and providing a written counteroffer and justification for such offer, including considerations based on the negotiation factors.

[3] The MFP is expressed as the price per 30-days equivalent supply. See section 60.1 of the revised guidance and the Negotiated Prices for Initial Price Applicability Year 2026 Fact Sheet for additional information.

[4] The Negotiation Program information collection request is available on the Office of Management and Budget's (OMB's) website at the following link: https://www.reginfo.gov/public/do/PRAViewICR?ref_nbr=202306-0938-013.

[5] Section 1194(e) of the Act requires CMS to consider certain data as the basis for all offers and counteroffers in the negotiation. These data, which are referred to in this document as the "negotiation factors," are discussed in more detail later in this document. More information on the negotiation factors is also available in sections 50, 60.3 and 60.4 of the revised guidance. CMS' p

CMS considered each counteroffer proposed by the Primary Manufacturers and declined each counteroffer. CMS and each Primary Manufacturer then held three negotiation meetings. These meetings included extensive discussion of the negotiation factors, including any new information consistent with the factors that may have become available about the selected drugs or therapeutic alternatives, CMS' initial offer and the Primary Manufacturer's written counteroffer, and, in some cases, additional proposals for an MFP.

Across the first cycle of negotiations for all ten selected drugs, more than 50 revised offers or counteroffers were proposed by CMS or a Primary Manufacturer, not including the ten initial offers CMS made and the ten written counteroffers provided by Primary Manufacturers. During the negotiation meetings, CMS revised its initial offer for each selected drug upwards at least once in response to the discussions with the Primary Manufacturer. While many of the details of the negotiations are confidential between CMS and each Primary Manufacturer, the frequency of revised offers and counteroffers in the first cycle of negotiations indicates the robustness of the negotiations that occurred for each of the ten drugs. CMS' approach to its negotiations with each Primary Manufacturer turned on the particular details relevant to each selected drug and was sensitive to the issues raised during the course of CMS' conversations with the Primary Manufacturer. CMS anticipates this drug-specific approach will continue to inform CMS' negotiations with participating manufacturers in future cycles of negotiation.

Overall, in six of ten negotiations CMS moved more than the Primary Manufacturer during the meetings and for the final offer (if applicable) prior to reaching agreement, and in four of ten negotiations the Primary Manufacturer moved more than CMS prior to reaching agreement. For five of the selected drugs, this process of exchanging revised offers and counteroffers resulted in CMS and the Primary Manufacturer reaching an agreement on a negotiated price for the selected drug in association with a negotiation meeting. In four of these cases, CMS accepted a revised counteroffer proposed by the Primary Manufacturer. For the remaining five selected drugs, CMS sent a written final offer to the Primary Manufacturer, consistent with the process described in the revised guidance, and in each instance, the Primary Manufacturer accepted CMS' offer on or before the statutory deadline. Throughout the negotiation process, CMS and the Primary Manufacturers exchanged perspectives about a range of topics related to the negotiation factors, and while the parties did not always agree, CMS appreciated the Primary Manufacturers' engagement.

A detailed timeline of the negotiation process for Enbrel is below.

- August 29, 2023: CMS announced the 10 selected drugs for initial price applicability year 2026
- October 1, 2023: Deadline for the Primary Manufacturer to sign an agreement to participate in the Negotiation Program
- October 2, 2023: Deadline for the Primary Manufacturer and the public to submit information related to Enbrel in response to the Negotiation Program information collection request
- October 27, 2023: CMS met with the Primary Manufacturer regarding its response to the Negotiation Program information collection request
- October 31, 2023: CMS held a patient-focused listening session for Enbrel
- February 1, 2024: CMS provided the Primary Manufacturer with CMS' initial offer
- March 1, 2024: The Primary Manufacturer rejected CMS' initial offer and provided CMS with a counteroffer
- March 29, 2024: CMS rejected the Primary Manufacturer's counteroffer and invited the Primary Manufacturer to a negotiation meeting
- May 2, 2024: CMS and the Primary Manufacturer met for the first negotiation meeting

- May 23, 2024: CMS and the Primary Manufacturer met for the second negotiation meeting
- June 20, 2024: CMS and the Primary Manufacturer met for the third negotiation meeting
- August 1, 2024: The negotiation period ended
- August 15, 2024: MFP of $2,355.00 was published

Indications for Enbrel

Enbrel is a drug that works by blocking the action of tumor necrosis factor, a protein in the body that causes inflammation. In people with certain autoimmune disorders, such as rheumatoid arthritis (RA), psoriatic arthritis, plaque psoriasis, and ankylosing spondylitis (AS), the body's immune system may be overactive and mistakenly attack healthy joints, skin, and/or other body systems leading to excess inflammation that can cause pain and damage to these systems.[6]

For Enbrel, CMS included the following indications in its assessment[7]:

Description of indication	Terminology used in this document
• To reduce the signs and symptoms, induce major clinical response, inhibit the progression of structural damage, and improve physical function in patients with moderately to severely active rheumatoid arthritis.	RA
• To reduce the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older.	pJIA
• To reduce the signs and symptoms, inhibit the progression of structural damage of active arthritis, and improve physical function in adult patients with psoriatic arthritis. • For the treatment of active juvenile psoriatic arthritis in pediatric patients 2 years of age and older.	Psoriatic arthritis
• To reduce the signs and symptoms in patients with active ankylosing spondylitis.	AS

[6] To compose this brief description, CMS used various sources, including MedlinePlus, a free online health information resource for patients and the general public. MedlinePlus is a service of the National Library of Medicine (NLM), a part of the U.S. National Institutes of Health (NIH). For more information about any drugs or conditions mentioned in this doc https://medlineplus.gov/.

[7] CMS' process for identifying indications for a selected drug was to identify the FDA-approved indication(s) not otherwise excluded from coverage or otherwise restricted under section 1860D-2(e)(2) of the Act, using prescribing information approved by the FDA for the selected drug, in accordance with section 1194(e)(2)(B) of the Act. CMS considered off-label use when identifying indications if such use was included in nationally recognized, evidence-based guidelines and recognized in CMS-approved Part D compendia. CMS included indications that met these criteria during the negotiation period. Indications newly approved by FDA or included in nationally recognized, evidence-based guidelines and recognized in CMS-approved Part D compendia after the end of the negotiation period were not included.

Description of indication	Terminology used in this document
• For the treatment of patients 4 years or older with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.	Plaque psoriasis

Table 1. AS = ankylosing spondylitis; pJIA = polyarticular juvenile idiopathic arthritis; RA = rheumatoid arthritis. For purposes of CMS' consideration of indications for Enbrel, CMS grouped certain indications using the terminology as shown in this table. CMS' use of the terms listed here does not alter the FDA-approved indications for Enbrel.

Factors Applied

Consistent with the IRA, CMS considered certain negotiation factors as the basis for determining all offers and counteroffers during the negotiation process.

The following negotiation factors are referred to in this document as "manufacturer-specific data"[8]:

- Research and development (R&D) costs of the Primary Manufacturer for Enbrel and the extent to which the Primary Manufacturer has recouped R&D costs;
- Current unit costs of production and distribution of Enbrel;
- Prior Federal financial support for novel therapeutic discovery and development with respect to Enbrel;
- Data on pending and approved patent applications, exclusivities recognized by the FDA, and applications and approvals for New Drug Applications and Biologics License Applications for Enbrel;[9] and
- Market data and revenue and sales volume data for Enbrel in the United States (U.S.).

The following negotiation factors are referred to in this document as "evidence about Enbrel and therapeutic alternatives to Enbrel"[10]:

- The extent to which Enbrel represents a therapeutic advance as compared to existing therapeutic alternatives and the costs of such existing therapeutic alternatives;
- Prescribing information approved by the FDA for Enbrel and therapeutic alternatives to Enbrel;
- Comparative effectiveness of Enbrel and therapeutic alternatives to Enbrel, taking into consideration the effects of Enbrel and therapeutic alternatives to Enbrel on specific populations, such as individuals with disabilities, the elderly, the terminally ill, children, and other patient populations; and
- The extent to which Enbrel and therapeutic alternatives to Enbrel address unmet medical needs for a condition for which treatment or diagnosis is not addressed adequately by available therapy.

[8] These factors are listed at section 1194(e)(1) of the Act.

[9] New Drug Applications are approved under section 505(c) of the Federal Food, Drug, and Cosmetic Act and Biologics License Applications are approved under section 351(a) of the Public Health Service Act.

[10] These factors are listed at section 1194(e)(2) of the Act. In accordance with section 1194(e)(2) and section 1182(e) of Title XI of the Act, CMS did not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, non-disabled, or not terminally ill, and, consistent with section 1182(e) of Title XI of the Act, did not use quality adjusted life years (QALYs).

The below sections describe how CMS considered and applied these factors during the negotiation process. CMS considered these factors, taking into account all data in totality during the negotiation process.

CMS and the Primary Manufacturer did not always agree on the information presented below, and the Primary Manufacturer was not restricted to consideration of these factors during the negotiation process but was free to discuss any topics with CMS it deemed relevant to its consideration of offer(s) and counteroffer(s) for Enbrel.

Manufacturer-Specific Data

CMS considered the information submitted by the Primary Manufacturer related to the manufacturer-specific data factors. These factors include R&D costs and the extent to which the Primary Manufacturer has recouped R&D costs, current unit costs of production and distribution, prior Federal financial support, data on pending and approved patents and exclusivities recognized by the FDA, and market data, including revenue and sales volume data for the drug in the United States. CMS considered these factors in totality, as part of its application of the negotiation factors during the negotiation process.

The Primary Manufacturer provided CMS with information for each of these factors in response to the Negotiation Program information collection request.[11] For R&D costs, CMS requested information separated into various categories of costs related to R&D, including acquisition costs, pre-clinical research costs, post-Investigational New Drug costs, costs of failed or abandoned products related to Enbrel, and other allowable direct costs. CMS also requested the global and U.S. total lifetime net revenue for Enbrel to provide insight into the extent to which the Primary Manufacturer has recouped R&D costs. CMS requested current average unit costs of production for Enbrel and current average unit costs of distribution for Enbrel separately, as well as a description of the methodology the Primary Manufacturer used to estimate such costs. For information related to prior Federal financial support, CMS requested the total amount of Federal financial support received, as well as a breakdown by various types of financial support, like tax credits and National Institutes of Health funding. CMS requested information on patents, both expired and unexpired, issued by the U.S. Patent and Trademark Office, patent applications, regulatory exclusivity periods, and active and pending FDA applications and approvals. For market data, CMS requested information about the prices for Enbrel and volume dispensed for other payers in the U.S. market, including commercial payers (e.g., the U.S. commercial average net price), Medicaid (Medicaid Best Price), and other Federal payers (the Federal supply schedule price and the Big Four price).

Throughout the negotiation process, CMS holistically considered the information submitted by the Primary Manufacturer related to the manufacturer-specific data negotiation factors for the purpose of negotiating an MFP for Enbrel. For example, CMS applied information on prices for Enbrel available to other payers in the U.S. market and how they compared to any offers or counteroffers when considering whether a potential price was consistent with CMS' aim to arrive at an agreement on the lowest possible MFP. The totality of CMS' application of these factors, in conjunction with application of the factors described below, informed CMS' negotiation of the MFP with the Primary Manufacturer.

[11] In accordance with the revised guidance, CMS treats R&D costs and the extent to which they are recouped, unit costs of production and distribution, pending patent applications, and market, revenue, and sales volume data as proprietary, unless the information that is provided to CMS is already publicly available. For more information, see section 40.2.1 of the revised guidance.

Evidence about Enbrel and Therapeutic Alternatives to Enbrel

CMS considered information related to the negotiation factors regarding evidence about Enbrel and therapeutic alternatives to Enbrel. CMS' holistic consideration of clinical benefit included evidence from sources such as: pivotal clinical trials, pre-specified subgroup analyses, clinical practice guidelines, expert consensus statements, comparative clinical evidence, published literature reviews, real-world evidence, and FDA prescription drug labeling, among others. CMS evaluated the evidence based on a variety of considerations, including relevance and credibility, giving priority to well-designed and well-conducted studies, as stated in the revised guidance.[12] In general, CMS prioritized direct comparative evidence (e.g., head-to-head randomized controlled trials) when available. CMS also reviewed mixed and/or indirect treatment comparisons (e.g., network meta-analyses) when available and real-world evidence (e.g., observational studies) when available as part of its holistic assessment of comparative evidence.

In addition to information from the Primary Manufacturer, CMS received information from the public, including from patients during the patient-focused listening session held by CMS on October 31, 2023.[13] Patient input was important to CMS' consideration of the evidence about Enbrel and therapeutic alternatives to Enbrel, including to help identify outcomes of interest for patients and to understand additional considerations such as patients' preferences with regard to potential treatments. For example, speakers at the patient-focused listening session shared that patients may respond differently to Enbrel and other treatments for autoimmune disorders, noting that an effective treatment for one patient may not be effective for another patient. This was one consideration among the many that informed CMS' understanding of the factors regarding evidence about Enbrel and its therapeutic alternatives. Throughout all of the patient-focused listening sessions for the first cycle of negotiations, speakers provided insight on the importance of affordability and access, which provided CMS helpful context for the speakers' described experiences.

Therapeutic Alternatives

The IRA directs CMS to compare Enbrel to therapeutic alternatives in its determination of offers and consideration of counteroffers for Enbrel.[14] In the revised guidance, CMS defines a therapeutic alternative for the first cycle of negotiations as a pharmaceutical product that is clinically comparable to the selected drug.[15]

Importantly, use of the term "therapeutic alternative" in this MFP explanation is limited to the purposes and definition outlined in the IRA and the revised guidance. Use of this term does not suggest that CMS believes such drugs are interchangeable or otherwise universally appropriate to prescribe for an

---

[12] In section 50.2 of the revised guidance, CMS stated, "When reviewing the literature from the public and manufacturer submissions as well as literature from CMS' review, CMS will consider the source, rigor of the study methodology, current relevance to the selected drug and its therapeutic alternative(s), whether the study has been through peer review, study limitations, degree of certainty of conclusions, risk of bias, study time horizons, generalizability, study population, and relevance to the negotiation factors listed in section 1194(e)(2) of the Act to ensure the integrity of the contributing data within the negotiation process. CMS will prioritize research, including both observational research and research based on randomized samples, that is methodologically rigorous, appropriately powered (i.e., has sufficient sample size) to answer the primary question of the research, and structured to avoid potential false positive findings due to multiple subgroup analyses."

[13] The redacted transcript f
https://www.cms.gov/files/document/enbrel-transcript-103123.pdf.

[14] See section 1194(e)(2) of the Act and sections 50, 60.3 and 60.4 of the revised guidance for additional information.

[15] This definition appears in Appendix C of the revised guidance.

individual in place of Enbrel or that these are the only pharmaceutical treatments that might be used by a person with one of the indications treated by Enbrel. CMS trusts that patients and health care providers will continue to choose the therapy that best suits a given patient's needs based on the patient's health, history, experience, and preferences, the provider's expertise, FDA-approved prescribing information, and relevant clinical guidelines, as applicable.

During the negotiation process, CMS identified therapeutic alternatives to Enbrel based on a holistic consideration of the available evidence from a range of sources. In addition to the sources listed above, such as data submitted by the Primary Manufacturer and the public and widely accepted clinical guidelines, other examples of data sources used include the following: drug classification systems commonly used in the public and commercial sector for formulary development, indications included in CMS-approved Part D compendia, and drug or drug class reviews.

The following table lists the therapeutic alternatives, among all clinically comparable alternatives that CMS reviewed, which were particularly relevant to CMS' consideration, due to guideline recommendations, utilization in the Medicare population, and other considerations.

Indication	Therapeutic Alternatives
RA	• Adalimumab • Infliximab
pJIA	• Adalimumab
Psoriatic Arthritis	• Adalimumab • Infliximab • Risankizumab • Secukinumab • Ustekinumab
AS	• Adalimumab • Infliximab
Plaque psoriasis	• Adalimumab • Infliximab • Risankizumab • Secukinumab • Ustekinumab

Table 2. AS = ankylosing spondylitis; pJIA = polyarticular juvenile idiopathic arthritis; RA = rheumatoid arthritis. Use of the term "therapeutic alternative" in this MFP explanation is limited to the purposes and definition outlined in the IRA and the revised guidance. Use of this term does not suggest that CMS believes such drugs are interchangeable or otherwise universally appropriate to prescribe for an individual in place of Enbrel or that these are the only pharmaceutical treatments that might be used by a person with one of the indications treated by Enbrel. CMS trusts that patients and health care providers will continue to choose the therapy that best suits a given patient's needs based on the patient's health, history, experience, and preferences, the provider's expertise, FDA-approved prescribing information, and relevant clinical guidelines, as applicable.

CMS considered utilization for Enbrel and its therapeutic alternatives by indication as one part of its application of the negotiation factors.

Outcomes and Additional Considerations

Outcomes are measurable effects or impacts of a treatment or intervention. Outcomes can be used to measure differences in the safety or effectiveness of different treatments. Patient-centered outcomes are outcomes identified by patients that are important to how they feel, function, or survive. To consider comparative effectiveness between Enbrel and therapeutic alternatives to Enbrel, CMS

identified clinically relevant and patient-centered outcomes of interest from the body of available literature to evaluate for each indication of Enbrel. CMS then identified evidence comparing Enbrel and its therapeutic alternatives based on these outcomes. The following table includes a non-exhaustive list of outcomes that were of interest to CMS in its consideration of Enbrel:

Indication	Effectiveness Outcomes	Safety Outcomes
RA	• Clinical response (e.g., ACR 20) • Disease activity (e.g., DAS 28) • Structural damage (e.g., radiographic non-progression) • Physical function (e.g., HAQ-DI) • HRQoL (e.g., SF-36)	• Serious adverse events • Tolerability (e.g., discontinuation due to adverse events)
pJIA	• Clinical response (e.g., pediatric core set of ACR response) • Disease activity (e.g., juvenile arthritis disease activity score) • Pain (e.g., VAS) • HRQoL (e.g, Child Health Questionnaire)	• Serious adverse events • Tolerability (e.g., discontinuation due to adverse events)
Psoriatic Arthritis	• Disease signs and symptoms (e.g., ACR 20; PASI 75) • Structural damage (e.g., radiographic non-progression) • Physical function (e.g., HAQ-DI) • HRQoL (e.g., Psoriatic Arthritis QOL)	• Serious adverse events • Tolerability (e.g., discontinuation due to adverse events)
AS	• Clinical response (e.g., ASAS 20) • Inflammation (e.g., CRP) • HRQoL (e.g., SF-36)	• Serious adverse events • Tolerability (e.g., discontinuation due to adverse events)
Plaque psoriasis	• Disease extent and severity (e.g., PASI 75) • HRQoL (e.g., DLQI)	• Serious adverse events • Tolerability (e.g., discontinuation due to adverse events)

Table 3. ACR = American College of Rheumatology; AS = ankylosing spondylitis; CDAI = Clinical Disease Activity Index; CRP = C-reactive protein; DAS = Disease Activity Score; DLQI = Dermatology Life Quality Index Questionnaire; HAQ-DI = Health Assessment Questionnaire - Disability Index; HRQoL = Health-related quality of life; PASI = Psoriasis Area and Severity Index; pJIA = polyarticular juvenile idiopathic arthritis; QoL = Quality of Life; RA = rheumatoid arthritis; SF-36 = 36-Item Short Form Survey. Outcomes identified in this table were of interest to CMS in its evaluation of Enbrel. Evidence to support an assessment may not have been available for every outcome of interest.

Outcomes, like those listed above, were identified as being of interest to CMS based on their importance to patients and their ability to measure how effective and safe a drug is when used to treat these indications. For example, for RA, certain signs and symptoms of the disease, structural damage to joints, and impact on patients' physical functioning are key outcomes that are often used to evaluate the effectiveness of treatments. In addition, across indications, the risk of serious adverse events and

tolerability, or the degree to which patients can tolerate adverse events associated with taking a drug, are outcomes that reflect important safety considerations when evaluating drugs for these indications.

Additionally, CMS considered the extent to which Enbrel represents a therapeutic advance as compared to existing therapeutic alternatives, and the extent to which Enbrel and its therapeutic alternatives address an unmet medical need. CMS also evaluated access, equity, and health outcomes for specific populations (including individuals with disabilities, the elderly, individuals who are terminally ill, children, and other patient populations).

For the purpose of negotiating the MFP for Enbrel, CMS holistically considered the negotiation factors regarding evidence about Enbrel and its therapeutic alternatives, including consideration of the clinical benefit of Enbrel in the context of its therapeutic alternatives. For example, CMS applied its understanding of the comparative effectiveness of Enbrel and its therapeutic alternatives for each of the identified indications, as well as additional contextual considerations, when negotiating with the Primary Manufacturer. Examples of additional contextual considerations for Enbrel and its therapeutic alternatives include the treatment complexity of these drugs (e.g., route of administration and frequency), use in related co-occurring conditions (e.g., inflammatory bowel disease), and specific disease manifestations (such as scalp or nail involvement in patients with plaque psoriasis).

Throughout the negotiation process, including the development of the initial offer and in the consideration of any offers and counteroffers, CMS applied these and other factors regarding evidence about Enbrel and therapeutic alternatives. The totality of CMS' application of these factors, in conjunction with application of the manufacturer-submitted data negotiation factors described above, informed CMS' negotiation of the MFP with the Primary Manufacturer.

Citations to Data Reviewed during the Negotiation Process for Enbrel

CMS provides below a list of citations representative of evidence that CMS reviewed during the negotiation process, including citations provided by the Primary Manufacturer and the public in response to the Negotiation Program information collection request, those included in CMS' initial offer concise justification, and other citations which were considered during the evaluation of the Primary Manufacturer's counteroffer and during negotiation meetings.

Consistent with the IRA and section 1182(e) of Title XI of the Act, CMS did not use evidence from comparative clinical effectiveness research in a manner that treats extending the life of an individual who is elderly, disabled, or terminally ill as of lower value than extending the life of an individual who is younger, nondisabled, or not terminally ill, and, consistent with section 1182(e) of Title XI of the Act, did not use quality adjusted life years (QALYs). Inclusion on this list of a citation that contains such evidence does not mean that CMS used such evidence in the course of the negotiation.

This list is intended to provide insight into the range of evidence that various parties, including CMS and the Primary Manufacturer, identified as being relevant to the negotiation. This list does not represent the totality of evidence that CMS reviewed and considered as part of its holistic consideration of the negotiation factors in the determination of any offers and consideration of any counteroffers.

1. AbbVie Inc. Humira (adalimumab) [package insert]. U.S. Food and Drug Administration. Revised 2021 Feb. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125057s417lbl.pdf.
2. AbbVie Inc. Rinvoq (upadacitinib) [package insert]. U.S. Food and Drug Administration. Revised 2023 Jun. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/211675s017lbl.pdf.
3. AbbVie Inc. Skyrizi (risankizumab-rzaa) [package insert]. U.S. Food and Drug Administration. Revised 2024 Jun. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761105s029,761262s007lbl.pdf.
4. Akay A, Pekcanlar A, Bozdag KE, Altintas L, Karaman A. Assessment of depression in subjects with psoriasis vulgaris and lichen planus. J Eur Acad Dermatol Venereol. 2002;16(4):347-52. doi: 10.1046/j.1468-3083.2002.00467.x. PubMed PMID: 12224690.
5. Alenghat FJ. The Prevalence of Atherosclerosis in Those with Inflammatory Connective Tissue Disease by Race, Age, and Traditional Risk Factors. Sci Rep. 2016;6:20303. Epub 20160204. doi: 10.1038/srep20303. PubMed PMID: 26842423; PubMed Central PMCID: PMC4740809.
6. Allocati E, Godman B, Gobbi M, Garattini S, Banzi R. Switching Among Biosimilars: A Review of Clinical Evidence. Front Pharmacol. 2022;13:917814. Epub 20220824. doi: 10.3389/fphar.2022.917814. PubMed PMID: 36091837; PubMed Central PMCID: PMC9449694.
7. Amgen, Inc. Enbrel (etanercept) [package insert]. U.S. Food and Drug Administration. Revised 2023 Oct. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/103795s5595lbl.pdf.
8. Amgen, Inc. Enbrel (etanercept) [package insert]. U.S. Food and Drug Administration. Revised 2022 Jun. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103795Orig1s5590lbl.pdf.
9. Armstrong AW, Puig L, Joshi A, Skup M, Williams D, Li J, et al. Comparison of Biologics and Oral Treatments for Plaque Psoriasis: A Meta-analysis. JAMA Dermatol. 2020;156(3):258-69.

doi: 10.1001/jamadermatol.2019.4029. PubMed PMID: 32022825; PubMed Central PMCID: PMC7042876.

10. Atiqi S, Hooijberg F, Loeff FC, Rispens T, Wolbink GJ. Immunogenicity of TNF-Inhibitors. Front Immunol. 2020;11:312. Epub 20200226. doi: 10.3389/fimmu.2020.00312. PubMed PMID: 32174918; PubMed Central PMCID: PMC7055461.
11. Barber CEH, Lacaille D, Croxford R, Barnabe C, Marshall DA, Abrahamowicz M, et al. Investigating Associations Between Access to Rheumatology Care, Treatment, Continuous Care, and Healthcare Utilization and Costs Among Older Individuals With Rheumatoid Arthritis. J Rheumatol. 2023;50(5):617-24. Epub 20230115. doi: 10.3899/jrheum.220729. PubMed PMID: 36642438.
12. Barnard, Claire. 'The Great Debate': JAK Inhibitors Vs Biologics Following Methotrexate Failure In RA: [Internet]. [Cited 2023 Oct 1]. Available from: https://www.medwirenews.com/showcase/the-great-debate-jak-inhibitors-vs-biologics-following-methotrexate-failure-in-ra/#:~:text=In%20a%20poll%20submitted%20at,be%20used%20before%20TNF%20inhibitors .
13. Bathon JM, Fleischmann RM, Van der Heijde D, Tesser JR, Peloso PM, Chon Y, et al. Safety and efficacy of etanercept treatment in elderly subjects with rheumatoid arthritis. J Rheumatol. 2006;33(2):234-43. PubMed PMID: 16465653.
14. Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff MH, Keystone EC, et al. A comparison of etanercept and methotrexate in patients with early rheumatoid arthritis. N Engl J Med. 2000;343(22):1586-93. doi: 10.1056/nejm200011303432201. PubMed PMID: 11096165.
15. Bergman M, Zhou L, Patel P, Sawant R, Clewell J, Tundia N. Healthcare Costs of Not Achieving Remission in Patients with Rheumatoid Arthritis in the United States: A Retrospective Cohort Study. Adv Ther. 2021;38(5):2558-70. Epub 20210409. doi: 10.1007/s12325-021-01730-w. PubMed PMID: 33837497; PubMed Central PMCID: PMC8107161.
16. Bessette L, Khraishi M, Kivitz AJ, Kaliyaperumal A, Grantab R, Poulin-Costello M, et al. Single-Arm Study of Etanercept in Adult Patients with Moderate to Severe Rheumatoid Arthritis Who Failed Adalimumab Treatment. Rheumatol Ther. 2017;4(2):391-404. Epub 20170912. doi: 10.1007/s40744-017-0079-x. PubMed PMID: 28900875; PubMed Central PMCID: PMC5696291.
17. Biosimilars Interchangeability & Switching 2023. In: Westrich-Roberson T, McKibbin R, Spiegel A, Reilly M, editors. AIArthritis Voices 360 Main. Full Episode 88. Missouri: International Foundation for Autoimmune & Autoinflammatory Arthritis (AIArthritis); 2023.
18. Björnsson ES, Gunnarsson BI, Gröndal G, Jonasson JG, Einarsdottir R, Ludviksson BR, et al. Risk of drug-induced liver injury from tumor necrosis factor antagonists. Clin Gastroenterol Hepatol. 2015;13(3):602-8. Epub 20140815. doi: 10.1016/j.cgh.2014.07.062. PubMed PMID: 25131534.
19. Blauvelt A, Gooderham M, Griffiths CEM, Armstrong AW, Zhu B, Burge R, et al. Cumulative Clinical Benefits of Biologics in the Treatment of Patients with Moderate-to-Severe Psoriasis over 1 Year: a Network Meta-Analysis. Dermatol Ther (Heidelb). 2022;12(3):727-40. Epub 20220223. doi: 10.1007/s13555-022-00690-5. PubMed PMID: 35195887; PubMed Central PMCID: PMC8941028.
20. Blom M, Kievit W, Kuper HH, Jansen TL, Visser H, den Broeder AA, et al. Frequency and effectiveness of dose increase of adalimumab, etanercept, and infliximab in daily clinical practice. Arthritis Care Res (Hoboken). 2010;62(9):1335-41. doi: 10.1002/acr.20211. PubMed PMID: 20506128.

21. Bolge SC, Goren A, Tandon N. Reasons for discontinuation of subcutaneous biologic therapy in the treatment of rheumatoid arthritis: a patient perspective. Patient Prefer Adherence. 2015;9:121-31. Epub 20150120. doi: 10.2147/PPA.S70834. PubMed PMID: 25653505; PubMed Central PMCID: PMC4309782.
22. Bonafede M, Joseph GJ, Shah N, Princic N, Harrison DJ. Cost of tumor necrosis factor blockers per patient with rheumatoid arthritis in a multistate Medicaid population. Clinicoecon Outcomes Res. 2014;6:381-8. Epub 20140915. doi: 10.2147/ceor.S61445. PubMed PMID: 25246804; PubMed Central PMCID: PMC4168856.
23. Bonafede M, Tang DH, Wilson K, Huang A, Harrison DJ, Stolshek BS. Etanercept and ustekinumab dosing for psoriasis and psoriatic arthritis. The American journal of pharmacy benefits. 2017;9(5):150-4.
24. Bonafede MM, Gandra SR, Fox KM, Wilson KL. Tumor necrosis factor blocker dose escalation among biologic naive rheumatoid arthritis patients in commercial managed-care plans in the 2 years following therapy initiation. J Med Econ. 2012;15(4):635-43. Epub 20120301. doi: 10.3111/13696998.2012.667028. PubMed PMID: 22332705.
25. Bonovas S, Minozzi S, Lytras T, González-Lorenzo M, Pecoraro V, Colombo S, et al. Risk of malignancies using anti-TNF agents in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis: a systematic review and meta-analysis. Expert Opin Drug Saf. 2016;15(sup1):35-54. doi: 10.1080/14740338.2016.1238458. PubMed PMID: 27924644.
26. Bradway Robert A. Testimony of Robert A. Bradway Chairman and Chief Executive Officer Amgen Inc. Before the U.S. House Committee on Oversight and Reform. 2020. Available from: https://docs.house.gov/meetings/GO/GO00/20201001/111056/HHRG-116-GO00-Wstate-BradwayR-20201001.pdf
27. Braun J, McHugh N, Singh A, Wajdula JS, Sato R. Improvement in patient-reported outcomes for patients with ankylosing spondylitis treated with etanercept 50 mg once-weekly and 25 mg twice-weekly. Rheumatology (Oxford). 2007;46(6):999-1004. Epub 20070327. doi: 10.1093/rheumatology/kem069. PubMed PMID: 17389658.
28. Braun J, Pavelka K, Ramos-Remus C, Dimic A, Vlahos B, Freundlich B, Koenig AS. Clinical efficacy of etanercept versus sulfasalazine in ankylosing spondylitis subjects with peripheral joint involvement. J Rheumatol. 2012 Apr;39(4):836-40. doi: 10.3899/jrheum.110885. Epub 2012 Feb 15. PMID: 22337244.
29. Braun J, van der Horst-Bruinsma IE, Huang F, Burgos-Vargas R, Vlahos B, Koenig AS, et al. Clinical efficacy and safety of etanercept versus sulfasalazine in patients with ankylosing spondylitis: a randomized, double-blind trial. Arthritis Rheum. 2011;63(6):1543-51. doi: 10.1002/art.30223. PubMed PMID: 21630245.
30. Bristol-Myers Squibb Company. Orencia (abatacept) [package insert]. U.S. Food and Drug Administration. Revised 2021 Dec. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125118s240lbl.pdf.
31. Bröms G, Granath F, Ekbom A, Hellgren K, Pedersen L, Sørensen HT, et al. Low Risk of Birth Defects for Infants Whose Mothers Are Treated With Anti-Tumor Necrosis Factor Agents During Pregnancy. Clin Gastroenterol Hepatol. 2016;14(2):234-41.e1-5. Epub 20150912. doi: 10.1016/j.cgh.2015.08.039. PubMed PMID: 26375613.
32. Brot-Goldberg ZC, Burn S, Layton T, Vabson B. Rationing medicine through bureaucracy: authorization restrictions in Medicare. National Bureau of Economic Research; 2023 Jan. Report No. 30878. doi: 10.3386/w30878. Available from: https://www.nber.org/papers/w30878.
33. Cai XC, Ru Y, Liu L, Sun XY, Zhou YQ, Luo Y, et al. Efficacy and safety of biological agents for the treatment of pediatric patients with psoriasis: A bayesian analysis of six high-quality

randomized controlled trials. Front Immunol. 2022;13:896550. Epub 20220819. doi: 10.3389/fimmu.2022.896550. PubMed PMID: 36081503; PubMed Central PMCID: PMC9446895.

34. Caso F, Tasso M, Chimenti MS, Navarini L, Perricone C, Girolimetto N, et al. Late-Onset and Elderly Psoriatic Arthritis: Clinical Aspects and Management. Drugs Aging. 2019;36(10):909-25. doi: 10.1007/s40266-019-00688-3. PubMed PMID: 31250280.
35. Chandra A, Ippolito B. What Does the Inflation Reduction Act Mean for Patients and Physicians? NEJM Catalyst. 2023;4(10):CAT.23.0138. doi: doi:10.1056/CAT.23.0138.
36. Chen CI, Wang L, Wei W, Yuce H, Phillips K. Burden of rheumatoid arthritis among US Medicare population: co-morbidities, health-care resource utilization and costs. Rheumatol Adv Pract. 2018;2(1):rky005. Epub 20180221. doi: 10.1093/rap/rky005. PubMed PMID: 31431954; PubMed Central PMCID: PMC6649951.
37. Ciofoaia EI, Pillarisetty A, Constantinescu F. Health disparities in rheumatoid arthritis. Ther Adv Musculoskelet Dis. 2022;14:1759720x221137127. Epub 20221119. doi: 10.1177/1759720x221137127. PubMed PMID: 36419481; PubMed Central PMCID: PMC9677290.
38. Coates LC, Soriano ER, Corp N, Bertheussen H, Callis Duffin K, Campanholo CB, Chau J, Eder L, Fernández-Ávila DG, FitzGerald O, Garg A, Gladman DD, Goel N, Helliwell PS, Husni ME, Jadon DR, Katz A, Laheru D, Latella J, Leung YY, Lindsay C, Lubrano E, Mazzuoccolo LD, Mease PJ, O'Sullivan D, Ogdie A, Olsder W, Palominos PE, Schick L, Steinkoenig I, de Wit M, van der Windt DA, Kavanaugh A; GRAPPA Treatment Recommendations domain subcommittees. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA): updated treatment recommendations for psoriatic arthritis 2021. Nat Rev Rheumatol. 2022 Aug;18(8):465-479. doi: 10.1038/s41584-022-00798-0. Epub 2022 Jun 27. Erratum in: Nat Rev Rheumatol. 2022 Dec;18(12):734. doi: 10.1038/s41584-022-00861-w. PMID: 35761070; PMCID: PMC9244095.
39. Cohen S, Samad A, Karis E, Stolshek BS, Trivedi M, Zhang H, et al. Decreased Injection Site Pain Associated with Phosphate-Free Etanercept Formulation in Rheumatoid Arthritis or Psoriatic Arthritis Patients: A Randomized Controlled Trial. Rheumatol Ther. 2019;6(2):245-54. Epub 20190327. doi: 10.1007/s40744-019-0152-8. PubMed PMID: 30915626; PubMed Central PMCID: PMC6514022.
40. Curtis JR, Baddley JW, Yang S, Patkar N, Chen L, Delzell E, et al. Derivation and preliminary validation of an administrative claims-based algorithm for the effectiveness of medications for rheumatoid arthritis. Arthritis Res Ther. 2011;13(5):R155. Epub 20110920. doi: 10.1186/ar3471. PubMed PMID: 21933396; PubMed Central PMCID: PMC3308085.
41. Curtis JR, Chastek B, Becker L, Quach C, Harrison DJ, Yun H, et al. Cost and effectiveness of biologics for rheumatoid arthritis in a commercially insured population. J Manag Care Spec Pharm. 2015;21(4):318-29. doi: 10.18553/jmcp.2015.21.4.318. PubMed PMID: 25803765; PubMed Central PMCID: PMC10398240.
42. Curtis JR, Emery P, Karis E, Haraoui B, Bykerk V, Yen PK, et al. Etanercept or Methotrexate Withdrawal in Rheumatoid Arthritis Patients in Sustained Remission. Arthritis Rheumatol. 2021;73(5):759-68. Epub 20210324. doi: 10.1002/art.41589. PubMed PMID: 33205906; PubMed Central PMCID: PMC8251940.
43. Curtis JR, Schabert VF, Harrison DJ, Yeaw J, Korn JR, Quach C, et al. Estimating effectiveness and cost of biologics for rheumatoid arthritis: application of a validated algorithm to commercial insurance claims. Clin Ther. 2014;36(7):996-1004. Epub 20140708. doi: 10.1016/j.clinthera.2014.05.062. PubMed PMID: 25012729.

44. Curtis JR, Schabert VF, Yeaw J, Korn JR, Quach C, Harrison DJ, et al. Use of a validated algorithm to estimate the annual cost of effective biologic treatment for rheumatoid arthritis. J Med Econ. 2014;17(8):555-66. Epub 20140514. doi: 10.3111/13696998.2014.914031. PubMed PMID: 24754646.
45. Curtis JR, Stolshek B, Emery P, Haraoui B, Karis E, Kricorian G, et al. Effects of Disease-Worsening Following Withdrawal of Etanercept or Methotrexate on Patient-Reported Outcomes in Patients With Rheumatoid Arthritis: Results From the SEAM-RA Trial. J Clin Rheumatol. 2023;29(1):16-22. Epub 20221022. doi: 10.1097/RHU.0000000000001893. PubMed PMID: 36459119; PubMed Central PMCID: PMC9803379.
46. Curtis JR, Xie F, Yun H, Bernatsky S, Winthrop KL. Real-world comparative risks of herpes virus infections in tofacitinib and biologic-treated patients with rheumatoid arthritis. Ann Rheum Dis. 2016;75(10):1843-7. Epub 20160425. doi: 10.1136/annrheumdis-2016-209131. PubMed PMID: 27113415; PubMed Central PMCID: PMC5553444.
47. Davis J, Jr., Webb A, Lund S, Sack K. Results from an open-label extension study of etanercept in ankylosing spondylitis. Arthritis Rheum. 2004;51(2):302-4. doi: 10.1002/art.20241. PubMed PMID: 15077279.
48. Davis JC, van der Heijde DM, Braun J, Dougados M, Cush J, Clegg D, et al. Sustained durability and tolerability of etanercept in ankylosing spondylitis for 96 weeks. Ann Rheum Dis. 2005;64(11):1557-62. Epub 20050420. doi: 10.1136/ard.2004.035105. PubMed PMID: 15843448; PubMed Central PMCID: PMC1755272.
49. Davtyan A, Lee JJY, Eder L, Hawker GA, Luo J, Barber CEH, et al. The Effects of Continuity of Rheumatology Care on Emergency Department Utilization and Hospitalizations for Individuals With Early Rheumatoid Arthritis: A Population-Based Study. J Rheumatol. 2023;50(6):748-53. Epub 20230201. doi: 10.3899/jrheum.220996. PubMed PMID: 36725062.
50. de Vries AC, Thio HB, de Kort WJ, Opmeer BC, van der Stok HM, de Jong EM, et al. A prospective randomized controlled trial comparing infliximab and etanercept in patients with moderate-to-severe chronic plaque-type psoriasis: the Psoriasis Infliximab vs. Etanercept Comparison Evaluation (PIECE) study. Br J Dermatol. 2017;176(3):624-33. Epub 20170202. doi: 10.1111/bjd.14867. PubMed PMID: 27416891.
51. Deodhar A, Bitman B, Yang Y, Collier DH. The effect of etanercept on traditional metabolic risk factors for cardiovascular disease in patients with rheumatoid arthritis. Clin Rheumatol. 2016;35(12):3045-52. Epub 20161005. doi: 10.1007/s10067-016-3422-7. PubMed PMID: 27704313; PubMed Central PMCID: PMC5118390.
52. Deodhar A, Chakravarty SD, Cameron C, Peterson S, Hensman R, Fogarty S, et al. A systematic review and network meta-analysis of current and investigational treatments for active ankylosing spondylitis. Clin Rheumatol. 2020;39(8):2307-15. Epub 20200227. doi: 10.1007/s10067-020-04970-3. PubMed PMID: 32107666; PubMed Central PMCID: PMC7338808.
53. Di Minno MN, Iervolino S, Zincarelli C, Lupoli R, Ambrosino P, Pizzicato P, et al. Cardiovascular effects of Etanercept in patients with psoriatic arthritis: evidence from the cardiovascular risk in rheumatic diseases database. Expert Opin Drug Saf. 2015;14(12):1905-13. Epub 20151130. doi: 10.1517/14740338.2015.1111870. PubMed PMID: 26618553.
54. Diav-Citrin O, Otcheretianski-Volodarsky A, Shechtman S, Ornoy A. Pregnancy outcome following gestational exposure to TNF-alpha-inhibitors: a prospective, comparative, observational study. Reprod Toxicol. 2014;43:78-84. Epub 20131124. doi: 10.1016/j.reprotox.2013.11.004. PubMed PMID: 24284028.

55. Dougados MR, van der Heijde DM, Brault Y, Koenig AS, Logeart IS. When to adjust therapy in patients with rheumatoid arthritis after initiation of etanercept plus methotrexate or methotrexate alone: findings from a randomized study (COMET). J Rheumatol. 2014;41(10):1922-34. Epub 20140815. doi: 10.3899/jrheum.131238. PubMed PMID: 25128520.
56. Duncan PB, Martin L, Ferdinand KC, Puckrein GA, Ahmed CD, Ross J, et al. Identifying How Prior Authorization Impacts Treatment of Underserved and Minority Patients. Association of Black Cardiologists, Inc.; Winter 2019. Available from: https://abcardio.org/wp-content/uploads/2019/03/AB-20190227-PA-White-Paper-Survey-Results-final.pdf.
57. Eli Lilly and Company. Olumiant (baricitinib) [package insert]. U.S. Food and Drug Administration. Revised 2022 Jun. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/207924s007lbl.pdf.
58. Eli Lilly and Company. Taltz (ixekizumab) [package insert]. U.S. Food and Drug Administration. Revised 2024 Aug. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/125521s032lbl.pdf.
59. Emery P, Breedveld F, van der Heijde D, Ferraccioli G, Dougados M, Robertson D, et al. Two-year clinical and radiographic results with combination etanercept-methotrexate therapy versus monotherapy in early rheumatoid arthritis: a two-year, double-blind, randomized study. Arthritis Rheum. 2010;62(3):674-82. doi: 10.1002/art.27268. PubMed PMID: 20187135.
60. Emery P, Breedveld FC, Hall S, Durez P, Chang DJ, Robertson D, et al. Comparison of methotrexate monotherapy with a combination of methotrexate and etanercept in active, early, moderate to severe rheumatoid arthritis (COMET): a randomised, double-blind, parallel treatment trial. Lancet. 2008;372(9636):375-82. Epub 20080716. doi: 10.1016/S0140-6736(08)61000-4. PubMed PMID: 18635256.
61. Emery P, Hammoudeh M, FitzGerald O, Combe B, Martin-Mola E, Buch MH, et al. Sustained remission with etanercept tapering in early rheumatoid arthritis. N Engl J Med. 2014;371(19):1781-92. doi: 10.1056/NEJMoa1316133. PubMed PMID: 25372086.
62. Emery P, Kvien TK, Combe B, Freundlich B, Robertson D, Ferdousi T, et al. Combination etanercept and methotrexate provides better disease control in very early (<=4 months) versus early rheumatoid arthritis (>4 months and <2 years): post hoc analyses from the COMET study. Ann Rheum Dis. 2012;71(6):989-92. Epub 20120308. doi: 10.1136/annrheumdis-2011-201066. PubMed PMID: 22402142.
63. Enbrel (etanercept) [FDA approval letter]. U.S. Food and Drug Administration; 1998 Nov 2. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/1998/etanimm110298L.htm.
64. Enbrel (etanercept) [FDA approval letter]. U.S. Food and Drug Administration; 1999 May 27. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/1999/etanimm052799L.htm.
65. Enbrel (etanercept) [FDA approval letter]. U.S. Food and Drug Administration; 2002 Jan 15. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2002/etanimm011502L.htm.
66. Enbrel (etanercept) [FDA approval letter]. U.S. Food and Drug Administration; 2004 Apr 30. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/biologics/2004/103795_5149ltr. pdf.

67. Enbrel (etanercept) Approval for ankylosing spondylitis. [FDA approval letter]. U.S. Food and Drug Administration; 2003 July 24. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2003/103795-5123ltr.pdf.
68. Enbrel (etanercept) Expanded approval for rheumatoid arthritis. [FDA approval letter]. U.S. Food and Drug Administration; 2003 July 24. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2003/103795-5097ltr.pdf.
69. Esposito M, Giunta A, Mazzotta A, Zangrilli A, Babino G, Bavetta M, et al. Efficacy and safety of subcutaneous anti-tumor necrosis factor-alpha agents, etanercept and adalimumab, in elderly patients affected by psoriasis and psoriatic arthritis: an observational long-term study. Dermatology. 2012;225(4):312-9. Epub 20121228. doi: 10.1159/000345623. PubMed PMID: 23295383.
70. Feldman SR, Kimball AB, Krueger GG, Woolley JM, Lalla D, Jahreis A. Etanercept improves the health-related quality of life of patients with psoriasis: results of a phase III randomized clinical trial. J Am Acad Dermatol. 2005;53(5):887-9. doi: 10.1016/j.jaad.2005.06.053. PubMed PMID: 16243150.
71. Feldmann M. Development of anti-TNF therapy for rheumatoid arthritis. Nature reviews Immunology. 2002;2(5):364-71. doi: 10.1038/nri802.
72. Felson DT, Anderson JJ, Boers M, Bombardier C, Chernoff M, Fried B, et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. The Committee on Outcome Measures in Rheumatoid Arthritis Clinical Trials. Arthritis Rheum. 1993;36(6):729-40. doi: 10.1002/art.1780360601. PubMed PMID: 8507213.
73. Ferreira BI, Abreu JL, Reis JP, Figueiredo AM. Psoriasis and Associated Psychiatric Disorders: A Systematic Review on Etiopathogenesis and Clinical Correlation. J Clin Aesthet Dermatol. 2016;9(6):36-43. Epub 20160601. PubMed PMID: 27386050; PubMed Central PMCID: PMC4928455.
74. Fleischmann RM, Baumgartner SW, Tindall EA, Weaver AL, Moreland LW, Schiff MH, et al. Response to etanercept (Enbrel) in elderly patients with rheumatoid arthritis: a retrospective analysis of clinical trial results. J Rheumatol. 2003;30(4):691-6. PubMed PMID: 12672185.
75. Fraenkel L, Bathon JM, England BR, St Clair EW, Arayssi T, Carandang K, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2021;73(7):924-39. Epub 20210608. doi: 10.1002/acr.24596. PubMed PMID: 34101387; PubMed Central PMCID: PMC9273041.
76. Frazier-Mironer A, Dougados M, Mariette X, Cantagrel A, Deschamps V, Flipo RM, et al. Retention rates of adalimumab, etanercept and infliximab as first and second-line biotherapy in patients with rheumatoid arthritis in daily practice. Joint Bone Spine. 2014;81(4):352-9. Epub 20140408. doi: 10.1016/j.jbspin.2014.02.014. PubMed PMID: 24721422.
77. Gabriel SE, Michaud K. Epidemiological studies in incidence, prevalence, mortality, and comorbidity of the rheumatic diseases. Arthritis Res Ther. 2009;11(3):229. Epub 20090519. doi: 10.1186/ar2669. PubMed PMID: 19519924; PubMed Central PMCID: PMC2714099.
78. Genentech, Inc. Actemra (tocilizumab) [package insert]. U.S. Food and Drug Administration. Revised 2022 Dec. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125276s138lbl.pdf.
79. Genentech, Inc. Rituxan (rituximab) [package insert]. U.S. Food and Drug Administration. Revised 2021 Dec. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103705s5467lbl.pdf.

80. Genovese MC, Bathon JM, Martin RW, Fleischmann RM, Tesser JR, Schiff MH, et al. Etanercept versus methotrexate in patients with early rheumatoid arthritis: two-year radiographic and clinical outcomes. Arthritis Rheum. 2002;46(6):1443-50. doi: 10.1002/art.10308. PubMed PMID: 12115173.
81. Genovese MC, Sanchez-Burson J, Oh M, Balazs E, Neal J, Everding A, et al. Comparative clinical efficacy and safety of the proposed biosimilar ABP 710 with infliximab reference product in patients with rheumatoid arthritis. Arthritis Res Ther. 2020;22(1):60. Epub 20200326. doi: 10.1186/s13075-020-2142-1. PubMed PMID: 32216829; PubMed Central PMCID: PMC7098142.
82. Gerriets V, Goyal A, Khaddour K. Tumor Necrosis Factor Inhibitors. [Updated 2023 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482425/.
83. Gharaibeh M, Bonafede M, McMorrow D, Hernandez EJM, Stolshek BS. Effectiveness and Costs Among Rheumatoid Arthritis Patients Treated with Targeted Immunomodulators Using Real-World U.S. Data. J Manag Care Spec Pharm. 2020;26(8):1039-49. doi: 10.18553/jmcp.2020.26.8.1039. PubMed PMID: 32715967; PubMed Central PMCID: PMC10398701.
84. Giusti K, Hamermesh RG, Krasnow M. Addressing Demographic Disparities in Clinical Trials. Harvard Business Review. 2021. Available from: https://hbr.org/2021/06/addressing-demographic-disparities-in-clinical-trials.
85. Gordon KB, Gottlieb AB, Leonardi CL, Elewski BE, Wang A, Jahreis A, et al. Clinical response in psoriasis patients discontinued from and then reinitiated on etanercept therapy. J Dermatolog Treat. 2006;17(1):9-17. doi: 10.1080/09546630500472838. PubMed PMID: 16467018.
86. Gorman JD, Sack KE, Davis JC. Treatment of Ankylosing Spondylitis by Inhibition of Tumor Necrosis Factor α. The New England journal of medicine. 2002;346(18):1349-56. doi: 10.1056/NEJMoa012664.
87. Greenberg JD, Reed G, Decktor D, Harrold L, Furst D, Gibofsky A, Dehoratius R, Kishimoto M, Kremer JM; CORRONA Investigators. A comparative effectiveness study of adalimumab, etanercept and infliximab in biologically naive and switched rheumatoid arthritis patients: results from the US CORRONA registry. Ann Rheum Dis. 2012 Jul;71(7):1134-42. doi: 10.1136/annrheumdis-2011-150573. Epub 2012 Jan 30. PMID: 22294625.
88. Griffiths CE, Strober BE, van de Kerkhof P, Ho V, Fidelus-Gort R, Yeilding N, et al. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. N Engl J Med. 2010;362(2):118-28. doi: 10.1056/NEJMoa0810652. PubMed PMID: 20071701.
89. Gu NY, Huang X-y. Claims Data Analysis of Dosing and Cost of TNF Antagonist. The American Journal of Pharmacy Benefits [Internet]. 2010. Available from: https://www.pharmacytimes.com/view/claims-data-analysis-of-dosing-and-cost-of-tnf-antagonist.
90. Gu T, Mutebi A, Stolshek BS, Tan H. Cost of biologic treatment persistence or switching in rheumatoid arthritis. Am J Manag Care. 2018;24(8 Spec No.):SP338-SP45. PubMed PMID: 30020745.
91. Gu T, Shah N, Deshpande G, Tang DH, Eisenberg DF, Harrison DJ. Biologic Cost per Effectively Treated Rheumatoid Arthritis Patient in a Large Managed Care Population: A Retrospective Cohort Study. J Health Econ Outcomes Res. 2016;3(2):122-31. Epub 20150917. doi: 10.36469/9830. PubMed PMID: 37663319; PubMed Central PMCID: PMC10471369.
92. Harigai M. Growing evidence of the safety of JAK inhibitors in patients with rheumatoid arthritis. Rheumatology (Oxford). 2019;58(Suppl 1):i34-i42. doi:

10.1093/rheumatology/key287. PubMed PMID: 30806708; PubMed Central PMCID: PMC6390880.

93. Hazlewood GS, Barnabe C, Tomlinson G, Marshall D, Devoe DJ, Bombardier C. Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying anti-rheumatic drugs for rheumatoid arthritis: A network meta-analysis. Cochrane Database Syst Rev. 2016;2016(8):Cd010227. Epub 20160829. doi: 10.1002/14651858.CD010227.pub2. PubMed PMID: 27571502; PubMed Central PMCID: PMC7087436.
94. Hetland ML, Christensen IJ, Tarp U, Dreyer L, Hansen A, Hansen IT, et al. Direct comparison of treatment responses, remission rates, and drug adherence in patients with rheumatoid arthritis treated with adalimumab, etanercept, or infliximab: results from eight years of surveillance of clinical practice in the nationwide Danish DANBIO registry. Arthritis Rheum. 2010;62(1):22-32. doi: 10.1002/art.27227. PubMed PMID: 20039405.
95. Hone D, Cheng A, Watson C, Huang B, Bitman B, Huang XY, et al. Impact of etanercept on work and activity impairment in employed moderate to severe rheumatoid arthritis patients in the United States. Arthritis Care Res (Hoboken). 2013;65(10):1564-72. doi: 10.1002/acr.22022. PubMed PMID: 23554320.
96. Hooper M, Wenkert D, Bitman B, Dias VC, Bartley Y. Malignancies in children and young adults on etanercept: summary of cases from clinical trials and post marketing reports. Pediatr Rheumatol Online J. 2013;11(1):35. Epub 20131002. doi: 10.1186/1546-0096-11-35. PubMed PMID: 24225257; PubMed Central PMCID: PMC3851136.
97. Horneff G, Burgos-Vargas R, Constantin T, Foeldvari I, Vojinovic J, Chasnyk VG, et al. Efficacy and safety of open-label etanercept on extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis and psoriatic arthritis: part 1 (week 12) of the CLIPPER study. Ann Rheum Dis. 2014;73(6):1114-22. Epub 20130521. doi: 10.1136/annrheumdis-2012-203046. PubMed PMID: 23696632; PubMed Central PMCID: PMC4033142.
98. Huang X, Gu NY, Fox KM, Harrison DJ, Globe D. Comparison of methods for measuring dose escalation of the subcutaneous TNF antagonists for rheumatoid arthritis patients treated in routine clinical practice. Curr Med Res Opin. 2010;26(7):1637-45. doi: 10.1185/03007995.2010.483127. PubMed PMID: 20429830.
99. Humira (adalimumab) [FDA approval letter]. U.S. Food and Drug Administration; 2008 Feb 21. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2008/125057s114ltr.pdf.
100. Humira (adalimumab) [FDA approval letter]. U.S. Food and Drug Administration; 2008 Jan 18. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2008/125057s0110ltr.pdf.
101. Humira (adalimumab) [package insert]. U.S. Food and Drug Administration. Revised 2006. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/125057s062lbl.pdf.
102. Janssen Biotech, Inc. Remicade (infliximab) [package insert]. U.S. Food and Drug Administration. Revised 2021 Oct. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/103772s5401lbl.pdf.
103. Janssen Biotech, Inc. Simponi (golimumab) [package insert]. U.S. Food and Drug Administration. Revised 2019 Sep. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125289s150lbl.pdf.
104. Janssen Biotech, Inc. Simponi Aria (golimumab) [package insert]. U.S. Food and Drug Administration. Revised 2021 Feb. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/125433s032lbl.pdf.

105. Janssen Biotech, Inc. Stelara (ustekinumab) [package insert]. U.S. Food and Drug Administration. Revised 2023 Mar. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125261s158lbl.pdf.
106. Janssen Biotech, Inc. Tremfya (guselkumab) [package insert]. U.S. Food and Drug Administration. Revised 2024 Sep. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761061s021lbl.pdf.
107. Joyce G, Blaylock B, Chen J, Van Nuys K. Medicare Part D plans greatly increased utilization restrictions on prescription drugs, 2011-20. Health Affairs. 2024 Mar; 43(3). doi: 10.1377/hlthaff.2023.00999. Available from: https://www.healthaffairs.org/doi/10.1377/hlthaff.2023.00999.
108. Kekow J, Moots RJ, Emery P, Durez P, Koenig A, Singh A, et al. Patient-reported outcomes improve with etanercept plus methotrexate in active early rheumatoid arthritis and the improvement is strongly associated with remission: the COMET trial. Ann Rheum Dis. 2010;69(1):222-5. doi: 10.1136/ard.2008.102509. PubMed PMID: 19293160.
109. Kelly C. Medicare-negotiated drugs may not get favorable coverage in Part D: will CMS intervene? [Internet]. Pink Sheet. 2024 Apr 16. Available from: https://insights.citeline.com/PS150091/Medicare-Negotiated-Drugs-May-Not-Get-Favorable-Coverage-In-Part-D-Will-CMS-Intervene/.
110. Kim H, Cho SK, Lee J, Bae SC, Sung YK. Increased risk of opportunistic infection in early rheumatoid arthritis. Int J Rheum Dis. 2019;22(7):1239-46. Epub 20190514. doi: 10.1111/1756-185x.13585. PubMed PMID: 31090187.
111. Kimball AB, Rothman KJ, Kricorian G, Pariser D, Yamauchi PS, Menter A, et al. OBSERVE-5: observational postmarketing safety surveillance registry of etanercept for the treatment of psoriasis final 5-year results. J Am Acad Dermatol. 2015;72(1):115-22. Epub 20140926. doi: 10.1016/j.jaad.2014.08.050. PubMed PMID: 25264239; PubMed Central PMCID: PMC4758511.
112. Kimball AB, Schenfeld J, Accortt NA, Anthony MS, Rothman KJ, Pariser D. Incidence rates of malignancies and hospitalized infectious events in patients with psoriasis with or without treatment and a general population in the U.S.A.: 2005-09. Br J Dermatol. 2014;170(2):366-73. doi: 10.1111/bjd.12744. PubMed PMID: 24251402.
113. Klareskog L, van der Heijde D, de Jager JP, Gough A, Kalden J, Malaise M, et al. Therapeutic effect of the combination of etanercept and methotrexate compared with each treatment alone in patients with rheumatoid arthritis: double-blind randomised controlled trial. Lancet. 2004;363(9410):675-81. doi: 10.1016/s0140-6736(04)15640-7. PubMed PMID: 15001324.
114. Klotsche J, Minden K, Thon A, Ganser G, Urban A, Horneff G. Improvement in health-related quality of life for children with juvenile idiopathic arthritis after start of treatment with etanercept. Arthritis Care Res (Hoboken). 2014;66(2):253-62. doi: 10.1002/acr.22112. PubMed PMID: 23983081.
115. Krishnan R, Cella D, Leonardi C, Papp K, Gottlieb AB, Dunn M, et al. Effects of etanercept therapy on fatigue and symptoms of depression in subjects treated for moderate to severe plaque psoriasis for up to 96 weeks. Br J Dermatol. 2007;157(6):1275-7. Epub 20071004. doi: 10.1111/j.1365-2133.2007.08205.x. PubMed PMID: 17916204.
116. Kristensen LE, Gülfe A, Saxne T, Geborek P. Efficacy and tolerability of anti-tumour necrosis factor therapy in psoriatic arthritis patients: results from the South Swedish Arthritis Treatment Group register. Ann Rheum Dis. 2008;67(3):364-9. Epub 20070720. doi: 10.1136/ard.2007.073544. PubMed PMID: 17644547.

117. Langley RG, Elewski BE, Lebwohl M, Reich K, Griffiths CE, Papp K, et al. Secukinumab in plaque psoriasis--results of two phase 3 trials. N Engl J Med. 2014;371(4):326-38. Epub 20140709. doi: 10.1056/NEJMoa1314258. PubMed PMID: 25007392.
118. Langley RG, Paller AS, Hebert AA, Creamer K, Weng HH, Jahreis A, et al. Patient-reported outcomes in pediatric patients with psoriasis undergoing etanercept treatment: 12-week results from a phase III randomized controlled trial. J Am Acad Dermatol. 2011;64(1):64-70. Epub 20100708. doi: 10.1016/j.jaad.2010.02.060. PubMed PMID: 20619489.
119. Leonardi CL, Powers JL, Matheson RT, Goffe BS, Zitnik R, Wang A, et al. Etanercept as monotherapy in patients with psoriasis. N Engl J Med. 2003;349(21):2014-22. doi: 10.1056/NEJMoa030409. PubMed PMID: 14627786.
120. Leonardi CL, See K, Burge R, Sun Z, Zhang Y, Mallbris L, et al. Number Needed to Treat Network Meta-Analysis to Compare Biologic Drugs for Moderate-to-Severe Psoriasis. Adv Ther. 2022;39(5):2256-69. Epub 20220322. doi: 10.1007/s12325-022-02065-w. PubMed PMID: 35316500; PubMed Central PMCID: PMC9056462.
121. Machado DA, Guzman RM, Xavier RM, Simon JA, Mele L, Pedersen R, et al. Open-label observation of addition of etanercept versus a conventional disease-modifying antirheumatic drug in subjects with active rheumatoid arthritis despite methotrexate therapy in the Latin American region. J Clin Rheumatol. 2014;20(1):25-33. doi: 10.1097/rhu.0000000000000055. PubMed PMID: 24356474.
122. Mahil SK, Ezejimofor MC, Exton LS, Manounah L, Burden AD, Coates LC, et al. Comparing the efficacy and tolerability of biologic therapies in psoriasis: an updated network meta-analysis. Br J Dermatol. 2020;183(4):638-49. Epub 20200809. doi: 10.1111/bjd.19325. PubMed PMID: 32562551.
123. Majka DS, Vu TT, Pope RM, Teodorescu M, Karlson EW, Liu K, et al. Association of Rheumatoid Factors With Subclinical and Clinical Atherosclerosis in African American Women: The Multiethnic Study of Atherosclerosis. Arthritis Care Res (Hoboken). 2017;69(2):166-74. doi: 10.1002/acr.22930. PubMed PMID: 27159164.
124. Maksymowych WP, Dougados M, van der Heijde D, Sieper J, Braun J, Citera G, et al. Clinical and MRI responses to etanercept in early non-radiographic axial spondyloarthritis: 48-week results from the EMBARK study. Ann Rheum Dis. 2016;75(7):1328-35. Epub 20150812. doi: 10.1136/annrheumdis-2015-207596. PubMed PMID: 26269397; PubMed Central PMCID: PMC4941178.
125. Marchesoni A, Zaccara E, Gorla R, Bazzani C, Sarzi-Puttini P, Atzeni F, et al. TNF-alpha antagonist survival rate in a cohort of rheumatoid arthritis patients observed under conditions of standard clinical practice. Ann N Y Acad Sci. 2009;1173:837-46. doi: 10.1111/j.1749-6632.2009.04621.x. PubMed PMID: 19758236.
126. Marotte H, Cimaz R. Etanercept - TNF receptor and IgG1 Fc fusion protein: is it different from other TNF blockers? Expert Opin Biol Ther. 2014 May;14(5):569-72. doi: 10.1517/14712598.2014.896334. Epub 2014 Mar 10. PMID: 24611432.
127. Martín-Mola E, Sieper J, Leirisalo-Repo M, Dijkmans BA, Vlahos B, Pedersen R, et al. Sustained efficacy and safety, including patient-reported outcomes, with etanercept treatment over 5 years in patients with ankylosing spondylitis. Clin Exp Rheumatol. 2010;28(2):238-45. Epub 20100513. PubMed PMID: 20483046.
128. Matsson A, Solomon DH, Crabtree MM, Harrison RW, Litman HJ, Johansson FD. Patterns in the sequential treatment of rheumatoid arthritis patients starting a b/tsDMARD: 10-year experience from a US-based registry. Res Sq. 2023. Epub 20230227. doi: 10.21203/rs.3.rs-2624931/v1. PubMed PMID: 36909600; PubMed Central PMCID: PMC10002849.

129. McInnes IB, Sawyer LM, Markus K, LeReun C, Sabry-Grant C, Helliwell PS. Targeted systemic therapies for psoriatic arthritis: a systematic review and comparative synthesis of short-term articular, dermatological, enthesitis and dactylitis outcomes. RMD Open. 2022;8(1). doi: 10.1136/rmdopen-2021-002074. PubMed PMID: 35321874; PubMed Central PMCID: PMC8943739.
130. Mease PJ, Gladman DD, Collier DH, Ritchlin CT, Helliwell PS, Liu L, et al. Etanercept and Methotrexate as Monotherapy or in Combination for Psoriatic Arthritis: Primary Results From a Randomized, Controlled Phase III Trial. Arthritis Rheumatol. 2019;71(7):1112-24. Epub 20190528. doi: 10.1002/art.40851. PubMed PMID: 30747501; PubMed Central PMCID: PMC6618246.
131. Mease PJ, Goffe BS, Metz J, VanderStoep A, Finck B, Burge DJ. Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised trial. Lancet. 2000;356(9227):385-90. doi: 10.1016/s0140-6736(00)02530-7. PubMed PMID: 10972371.
132. Mease PJ, Kivitz AJ, Burch FX, Siegel EL, Cohen SB, Ory P, et al. Continued inhibition of radiographic progression in patients with psoriatic arthritis following 2 years of treatment with etanercept. J Rheumatol. 2006;33(4):712-21. Epub 20060201. PubMed PMID: 16463435.
133. Mease PJ, Kivitz AJ, Burch FX, Siegel EL, Cohen SB, Ory P, et al. Etanercept treatment of psoriatic arthritis: safety, efficacy, and effect on disease progression. Arthritis Rheum. 2004;50(7):2264-72. doi: 10.1002/art.20335. PubMed PMID: 15248226.
134. Mease PJ, McInnes IB, Tam LS, Rajalingam R, Peterson S, Hassan F, et al. Comparative effectiveness of guselkumab in psoriatic arthritis: updates to a systematic literature review and network meta-analysis. Rheumatology (Oxford). 2023;62(4):1417-25. doi: 10.1093/rheumatology/keac500. PubMed PMID: 36102818; PubMed Central PMCID: PMC10070072.
135. Mease PJ, Woolley JM, Singh A, Tsuji W, Dunn M, Chiou CF. Patient-reported outcomes in a randomized trial of etanercept in psoriatic arthritis. J Rheumatol. 2010;37(6):1221-7. Epub 20100415. doi: 10.3899/jrheum.091093. PubMed PMID: 20395648.
136. Medicare Advantage. The Henry J. Kaiser Family Foundation; 2017 October 10. Available from: https://web.archive.org/web/20171010191924/https://www.kff.org/medicare/fact-sheet/medicare-advantage/
137. Menter A, Cordoro KM, Davis DMR, Kroshinsky D, Paller AS, Armstrong AW, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients. J Am Acad Dermatol. 2020;82(1):161-201. Epub 20191105. doi: 10.1016/j.jaad.2019.08.049. PubMed PMID: 31703821.
138. Menter A, Gelfand JM, Connor C, Armstrong AW, Cordoro KM, Davis DMR, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management of psoriasis with systemic nonbiologic therapies. J Am Acad Dermatol. 2020;82(6):1445-86. Epub 20200228. doi: 10.1016/j.jaad.2020.02.044. PubMed PMID: 32119894.
139. Menter A, Strober BE, Kaplan DH, Kivelevitch D, Prater EF, Stoff B, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029-72. Epub 20190213. doi: 10.1016/j.jaad.2018.11.057. PubMed PMID: 30772098.
140. Mercer LK, Lunt M, Low AL, Dixon WG, Watson KD, Symmons DP, et al. Risk of solid cancer in patients exposed to anti-tumour necrosis factor therapy: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Ann Rheum Dis. 2015;74(6):1087-

93. Epub 20140331. doi: 10.1136/annrheumdis-2013-204851. PubMed PMID: 24685910; PubMed Central PMCID: PMC4431340.

141. Militello G, Xia A, Stevens SR, Van Voorhees AS. Etanercept for the treatment of psoriasis in the elderly. J Am Acad Dermatol. 2006;55(3):517-9. doi: 10.1016/j.jaad.2006.02.010. PubMed PMID: 16908365.

142. Moderate to Severe Plaque Psoriasis: Efficacy Data [Internet]. Amgen, Inc; 2024. Available from: https://www.enbrelpro.com/efficacy/plaque-psoriasis.

143. Møller AH, Erntoft S, Vinding GR, Jemec GB. A systematic literature review to compare quality of life in psoriasis with other chronic diseases using EQ-5D-derived utility values. Patient Relat Outcome Meas. 2015;6:167-77. Epub 20150707. doi: 10.2147/prom.S81428. PubMed PMID: 26185476; PubMed Central PMCID: PMC4500621.

144. Moots RJ, Haraoui B, Matucci-Cerinic M, van Riel PL, Kekow J, Schaeverbeke T, et al. Differences in biologic dose-escalation, non-biologic and steroid intensification among three anti-TNF agents: evidence from clinical practice. Clin Exp Rheumatol. 2011;29(1):26-34. Epub 20110223. PubMed PMID: 21345289.

145. Moots RJ, Mays R, Stephens J, Tarallo M. Burden of dose escalation with tumour necrosis factor inhibitors in rheumatoid arthritis: a systematic review of frequency and costs. Clin Exp Rheumatol. 2015;33(5):737-45. Epub 20150608. PubMed PMID: 26053198.

146. Moreland LW, Schiff MH, Baumgartner SW, Tindall EA, Fleischmann RM, Bulpitt KJ, et al. Etanercept therapy in rheumatoid arthritis. A randomized, controlled trial. Ann Intern Med. 1999;130(6):478-86. doi: 10.7326/0003-4819-130-6-199903160-00004. PubMed PMID: 10075615.

147. Mougui A, Baba Z, Hmamouchi I, Abouqal R, Bezza A, Allali F, et al. Characteristics of Late-Onset Spondyloarthritis: Data from the Moroccan Registry of Biological Therapies in Rheumatic Diseases. Cureus. 2023;15(5):e39100. Epub 20230516. doi: 10.7759/cureus.39100. PubMed PMID: 37273389; PubMed Central PMCID: PMC10234029.

148. Mourad AI, Gniadecki R. Biologic Drug Survival in Psoriasis: A Systematic Review & Comparative Meta-Analysis. Front Med (Lausanne). 2020;7:625755. Epub 20210318. doi: 10.3389/fmed.2020.625755. PubMed PMID: 33816514; PubMed Central PMCID: PMC8012481.

149. Murdaca G, Spano F, Contatore M, Guastalla A, Penza E, Magnani O, et al. Immunogenicity of infliximab and adalimumab: what is its role in hypersensitivity and modulation of therapeutic efficacy and safety? Expert Opin Drug Saf. 2016;15(1):43-52. Epub 20151111. doi: 10.1517/14740338.2016.1112375. PubMed PMID: 26559805.

150. Myasoedova E, Crowson CS, Kremers HM, Therneau TM, Gabriel SE. Is the incidence of rheumatoid arthritis rising?: results from Olmsted County, Minnesota, 1955-2007. Arthritis Rheum. 2010;62(6):1576-82. doi: 10.1002/art.27425. PubMed PMID: 20191579; PubMed Central PMCID: PMC2929692.

151. Narbutt J, Niedzwiedz M, Lesiak A, Ceryn J, Skibinska M. Secukinumab for the Treatment of Psoriasis in Pediatrics: Patient Selection and Acceptability. Patient Prefer Adherence. 2023;17:421-31. Epub 20230216. doi: 10.2147/PPA.S350753. PubMed PMID: 36815128; PubMed Central PMCID: PMC9940655.

152. Nash P, Dutz JP, Peterson S, Patel BP, Eaton K, Shawi M, et al. Systematic literature review and network meta-analysis of therapies for psoriatic arthritis on patient-reported outcomes. BMJ Open. 2023;13(11):e062306. Epub 20231108. doi: 10.1136/bmjopen-2022-062306. PubMed PMID: 37940157; PubMed Central PMCID: PMC10632897.

153. National Institute of Allergy and Infectious Diseases. Overview of the Immune System [Internet]. Maryland: National Institutes of Health; 2013 [cited 2023 Oct 2]. Available from: https://www.niaid.nih.gov/research/immune-system-overview.
154. New Data Show Many Rheumatoid Arthritis Patients Treated With ENBREL Plus Methotrexate Have Experienced Clinical Remission and Most Had No Progression of Joint Damage: [Internet]. California: Amgen Inc [cited 2023 Oct 2]. Available from: https://www.amgen.com/newsroom/press-releases/2003/10/new-data-show-many-rheumatoid-arthritis-patients-treated-with-enbrel-plus-methotrexate-have-experienced-clinical-remission-and-most-had-no-progression-of-joint-damage#:~:text=THOUSAND%20OAKS%2C%20Calif.,Activity%20Score%20(DAS)%20criteria.
155. Novartis Pharmaceuticals Corporation. Cosentyx (secukinumab) [package insert]. U.S. Food and Drug Administration. Revised 2023 May. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/125504s044lbl.pdf.
156. Nowell WB, Karis E, Gavigan K, Stradford L, Zhao H, Chen L, et al. Patient-Reported Nausea and Fatigue Related to Methotrexate: A Prospective, Self-Controlled Study in the ArthritisPower(®) Registry. Rheumatol Ther. 2022;9(1):207-21. Epub 20211128. doi: 10.1007/s40744-021-00398-6. PubMed PMID: 34843092; PubMed Central PMCID: PMC8628141.
157. Office of Inspector General. Some Medicare Part D beneficiaries face avoidable extra steps that can delay or prevent access to prescribed drugs; U.S. Department of Health and Human Services. 2019 Sep. Report No: OEI-09-16-00411. Available from: https://oig.hhs.gov/reports-and-publications/workplan/summary/wp-summary-0000297.asp.
158. Ollendorf DA, Chapman R, Pearson SD, Kumar V, Agboola F, Synnott P, et al. Targeted Immune Modulators for Rheumatoid Arthritis: Effectiveness & Value. Institute for Clinical and Economic Review (ICER), 2017. Available from: https://icer.org/wp-content/uploads/2020/10/NE_CEPAC_RA_Evidence_Report_FINAL_040717.pdf.
159. Ollendorf DA, Klingman D, Hazard E, Ray S. Differences in annual medication costs and rates of dosage increase between tumor necrosis factor-antagonist therapies for rheumatoid arthritis in a managed care population. Clin Ther. 2009;31(4):825-35. doi: 10.1016/j.clinthera.2009.04.002. PubMed PMID: 19446156.
160. Ozguler Y, Hatemi G, Ugurlu S, Seyahi E, Melikoglu M, Borekci S, et al. Re-initiation of biologics after the development of tuberculosis under anti-TNF therapy. Rheumatol Int. 2016;36(12):1719-25. Epub 20161003. doi: 10.1007/s00296-016-3575-3. PubMed PMID: 27699578.
161. Paller AS, Eichenfield LF, Langley RG, Leonardi CL, Siegfried EC, Creamer K, et al. Subgroup analyses of etanercept in pediatric patients with psoriasis. J Am Acad Dermatol. 2010;63(2):e38-41. doi: 10.1016/j.jaad.2009.11.001. PubMed PMID: 20633781.
162. Paller AS, Siegfried EC, Langley RG, Gottlieb AB, Pariser D, Landells I, et al. Etanercept treatment for children and adolescents with plaque psoriasis. N Engl J Med. 2008;358(3):241-51. doi: 10.1056/NEJMoa066886. PubMed PMID: 18199863.
163. Paller AS, Siegfried EC, Pariser DM, Rice KC, Trivedi M, Iles J, et al. Long-term safety and efficacy of etanercept in children and adolescents with plaque psoriasis. J Am Acad Dermatol. 2016;74(2):280-7 e1-3. doi: 10.1016/j.jaad.2015.09.056. PubMed PMID: 26775775.
164. Papp K, Bachelez H, Costanzo A, Foley P, Gooderham M, Kaur P, et al. Clinical similarity of biosimilar ABP 501 to adalimumab in the treatment of patients with moderate to severe plaque psoriasis: A randomized, double-blind, multicenter, phase III study. J Am Acad

Dermatol. 2017;76(6):1093-102. Epub 20170311. doi: 10.1016/j.jaad.2016.12.014. PubMed PMID: 28291552.

165. Papp KA, Tyring S, Lahfa M, Prinz J, Griffiths CE, Nakanishi AM, et al. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. Br J Dermatol. 2005;152(6):1304-12. doi: 10.1111/j.1365-2133.2005.06688.x. PubMed PMID: 15948997.
166. Patterson JA, Wagner TD, O'Brien JM, Campbell JD. Medicare Part D Coverage of Drugs Selected for the Drug Price Negotiation Program. JAMA Health Forum. 2024 Feb 2;5(2):e235237. doi: 10.1001/jamahealthforum.2023.5237. PMID: 38334994; PMCID: PMC10858397.
167. Pérez-Stable EJ, Valdez RO. Announcement of Decision to Designate People with Disabilities as a Population with Health Disparities: National Institute on Minority Health and Health Disparities; 2023 [updated 2023 Sep 28]. Available from: https://www.nimhd.nih.gov/about/directors-corner/messages/health-disparities-population-designation.html.
168. Pfizer, Inc. Xeljanz (tofacitinib) [package insert]. U.S. Food and Drug Administration. Revised 2020 Sep. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/203214s026lbl.pdf, https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213082s000lbl.pdf.
169. Pfizer, Inc. Xeljanz XR (tofacitinib) [package insert]. U.S. Food and Drug Administration. Revised 2021 Dec. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/208246s017,213082s004lbl.pdf.
170. Piragine E, Petri D, Martelli A, Janowska A, Dini V, Romanelli M, et al. Adherence and Persistence to Biological Drugs for Psoriasis: Systematic Review with Meta-Analysis. J Clin Med. 2022;11(6). Epub 20220309. doi: 10.3390/jcm11061506. PubMed PMID: 35329831; PubMed Central PMCID: PMC8953825.
171. Pope JE, Haraoui B, Thorne JC, Vieira A, Poulin-Costello M, Keystone EC. The Canadian methotrexate and etanercept outcome study: a randomised trial of discontinuing versus continuing methotrexate after 6 months of etanercept and methotrexate therapy in rheumatoid arthritis. Ann Rheum Dis. 2014;73(12):2144-51. Epub 20130826. doi: 10.1136/annrheumdis-2013-203684. PubMed PMID: 23979914; PubMed Central PMCID: PMC4251190.
172. Press Release: Amgen Launches The ENBREL Mini™ Single-Dose Prefilled Cartridge With AutoTouch™ Reusable Autoinjector That Is Ergonomically Designed For Patients [Internet]. Amgen, Inc; 2017. Available from: https://www.amgen.com/newsroom/press-releases/2017/11/amgen-launches-the-enbrel-mini-single-dose-prefilled-cartridge-with-autotouch-reusable-autoinjector-that-is-ergonomically-designed-for-patients.
173. Rákóczi É, Perge B, Végh E, Csomor P, Pusztai A, Szamosi S, et al. Evaluation of the immunogenicity of the 13-valent conjugated pneumococcal vaccine in rheumatoid arthritis patients treated with etanercept. Joint Bone Spine. 2016;83(6):675-9. Epub 20160316. doi: 10.1016/j.jbspin.2015.10.017. PubMed PMID: 26995488.
174. Remicade (infliximab) [FDA approval letter]. U.S. Food and Drug Administration; 2004 Dec 17. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2004/103772_5077_ltr.pdf.
175. Rheumatoid Arthritis [Internet]. Georgia: U.S. Centers for Disease Control and Prevention [cited 2023 Oct 2]. Available from: https://www.cdc.gov/arthritis/rheumatoid-arthritis/.

176. Ringold S, Angeles-Han ST, Beukelman T, Lovell D, Cuello CA, Becker ML, et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Non-Systemic Polyarthritis, Sacroiliitis, and Enthesitis. Arthritis Care Res (Hoboken). 2019;71(6):717-34. Epub 20190425. doi: 10.1002/acr.23870. PubMed PMID: 31021516; PubMed Central PMCID: PMC6561125.
177. Rodgers M, Epstein D, Bojke L, Yang H, Craig D, Fonseca T, et al. Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis: a systematic review and economic evaluation. Health Technol Assess. 2011;15(10):i-xxi, 1-329. doi: 10.3310/hta15100. PubMed PMID: 21333232; PubMed Central PMCID: PMC4781419.
178. Ruderman EM. Evaluation and management of psoriatic arthritis: the role of biologic therapy. J Am Acad Dermatol. 2003;49(2 Suppl):S125-32. doi: 10.1016/s0190-9622(03)01145-9. PubMed PMID: 12894136.
179. sanofi-aventis U.S. LLC. Kevzara (sarilumab) [package insert]. U.S. Food and Drug Administration. Revised 2023 Feb. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761037s013lbl.pdf.
180. Santos-Moreno P, Sánchez G, Gómez D, Bello-Gualtero J, Castro C. Direct Comparative Effectiveness Among 3 Anti-Tumor Necrosis Factor Biologics in a Real-Life Cohort of Patients With Rheumatoid Arthritis. J Clin Rheumatol. 2016;22(2):57-62. doi: 10.1097/rhu.0000000000000358. PubMed PMID: 26886438; PubMed Central PMCID: PMC4927323.
181. Sbidian E, Chaimani A, Guelimi R, Garcia-Doval I, Hua C, Hughes C, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2023;7(7):Cd011535. Epub 20230712. doi: 10.1002/14651858.CD011535.pub6. PubMed PMID: 37436070; PubMed Central PMCID: PMC10337265.
182. Schiff MH, Yu EB, Weinblatt ME, Moreland LW, Genovese MC, White B, et al. Long-term experience with etanercept in the treatment of rheumatoid arthritis in elderly and younger patients: patient-reported outcomes from multiple controlled and open-label extension studies. Drugs Aging. 2006;23(2):167-78. doi: 10.2165/00002512-200623020-00006. PubMed PMID: 16536638.
183. Schmajuk G, Trivedi AN, Solomon DH, Yelin E, Trupin L, Chakravarty EF, et al. Receipt of disease-modifying antirheumatic drugs among patients with rheumatoid arthritis in Medicare managed care plans. Jama. 2011;305(5):480-6. doi: 10.1001/jama.2011.67. PubMed PMID: 21285425; PubMed Central PMCID: PMC3172813.
184. Schmitz S, Adams R, Walsh CD, Barry M, FitzGerald O. A mixed treatment comparison of the efficacy of anti-TNF agents in rheumatoid arthritis for methotrexate non-responders demonstrates differences between treatments: a Bayesian approach. Ann Rheum Dis. 2012;71(2):225-30. Epub 20110929. doi: 10.1136/annrheumdis-2011-200228. PubMed PMID: 21960560.
185. Shah SK, Arthur A, Yang YC, Stevens S, Alexis AF. A retrospective study to investigate racial and ethnic variations in the treatment of psoriasis with etanercept. J Drugs Dermatol. 2011 Aug;10(8):866-72. PMID: 21818507.
186. Singh JA, Christensen R, Wells GA, Suarez-Almazor ME, Buchbinder R, Lopez-Olivo MA, et al. Biologics for rheumatoid arthritis: an overview of Cochrane reviews. Cochrane Database Syst Rev. 2009;2009(4):CD007848. Epub 20091007. doi: 10.1002/14651858.CD007848.pub2. PubMed PMID: 19821440; PubMed Central PMCID: PMC10636593.
187. Singh JA, Guyatt G, Ogdie A, Gladman DD, Deal C, Deodhar A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the

Treatment of Psoriatic Arthritis. Arthritis Rheumatol. 2019;71(1):5-32. Epub 20181130. doi: 10.1002/art.40726. PubMed PMID: 30499246; PubMed Central PMCID: PMC8218333.

188. Singh JA, Hossain A, Mudano AS, Tanjong Ghogomu E, Suarez-Almazor ME, Buchbinder R, et al. Biologics or tofacitinib for people with rheumatoid arthritis naive to methotrexate: a systematic review and network meta-analysis. Cochrane Database of Systematic Reviews. 2017(5). doi: 10.1002/14651858.CD012657. PubMed PMID: CD012657.
189. Singh JA, Hossain A, Tanjong Ghogomu E, Kotb A, Christensen R, Mudano AS, et al. Biologics or tofacitinib for rheumatoid arthritis in incomplete responders to methotrexate or other traditional disease-modifying anti-rheumatic drugs: a systematic review and network meta-analysis. Cochrane Database Syst Rev. 2016;2016(5):Cd012183. Epub 20160513. doi: 10.1002/14651858.Cd012183. PubMed PMID: 27175934; PubMed Central PMCID: PMC7068903.
190. Singh JA, Hossain A, Tanjong Ghogomu E, Mudano AS, Tugwell P, Wells GA. Biologic or tofacitinib monotherapy for rheumatoid arthritis in people with traditional disease-modifying anti-rheumatic drug (DMARD) failure: a Cochrane Systematic Review and network meta-analysis (NMA). Cochrane Database Syst Rev. 2016;11(11):CD012437. Epub 20161117. doi: 10.1002/14651858.CD012437. PubMed PMID: 27855242; PubMed Central PMCID: PMC6469573.
191. Smitten AL, Choi HK, Hochberg MC, Suissa S, Simon TA, Testa MA, et al. The risk of herpes zoster in patients with rheumatoid arthritis in the United States and the United Kingdom. Arthritis Rheum. 2007;57(8):1431-8. doi: 10.1002/art.23112. PubMed PMID: 18050184.
192. Song IH, Hermann KG, Haibel H, Althoff CE, Poddubnyy D, Listing J, et al. Consistently Good clinical response in patients with early axial spondyloarthritis after 3 years of continuous treatment with etanercept: longterm data of the ESTHER trial. J Rheumatol. 2014;41(10):2034-40. Epub 20140715. doi: 10.3899/jrheum.140056. PubMed PMID: 25028375.
193. Song IH, Hermann KG, Haibel H, Althoff CE, Poddubnyy D, Listing J, et al. Inflammatory and fatty lesions in the spine and sacroiliac joints on whole-body MRI in early axial spondyloarthritis--3-Year data of the ESTHER trial. Semin Arthritis Rheum. 2016;45(4):404-10. Epub 20150904. doi: 10.1016/j.semarthrit.2015.08.005. PubMed PMID: 26519007.
194. Sugihara T. Treatment strategies for elderly-onset rheumatoid arthritis in the new era. Mod Rheumatol. 2022;32(3):493-9. doi: 10.1093/mr/roab087. PubMed PMID: 34791359.
195. Sun Pharmaceutical Industries, Inc. Ilumya (tildrakizumab-asmn) [package insert]. U.S. Food and Drug Administration. Revised 2022 Dec. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761067s014lbl.pdf.
196. The Ethics of Step Therapy: Next Steps. Missouri: International Foundation for Autoimmune & Autoinflammatory Arthritis (AIArthritis), 2015. Available from: https://irp-cdn.multiscreensite.com/8f027529/files/uploaded/The%20Ethics%20of%20Step%20Therapy%202019.pdf.
197. Tkacz J, Gharaibeh M, DeYoung KH, Wilson K, Collier D, Oko-Osi H. Treatment Patterns and Costs in Biologic DMARD-Naive Patients with Rheumatoid Arthritis Initiating Etanercept or Adalimumab with or Without Methotrexate. J Manag Care Spec Pharm. 2020;26(3):285-94. doi: 10.18553/jmcp.2020.26.3.285. PubMed PMID: 32105179; PubMed Central PMCID: PMC10391042.
198. Tyring S, Gottlieb A, Papp K, Gordon K, Leonardi C, Wang A, et al. Etanercept and clinical outcomes, fatigue, and depression in psoriasis: double-blind placebo-controlled randomised phase III trial. Lancet. 2006;367(9504):29-35. doi: 10.1016/S0140-6736(05)67763-X. PubMed PMID: 16399150.

199. UCB, Inc. Cimzia (certolizumab pegol) [package insert]. U.S. Food and Drug Administration. Revised 2022 Dec. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125160s305lbl.pdf.
200. Upchurch KS, Kay J. Evolution of treatment for rheumatoid arthritis. Rheumatology (Oxford, England). 2012;51(6):vi28-vi36. doi: 10.1093/rheumatology/kes278.
201. Valeant Pharmaceuticals North America LLC. Siliq (brodalumab) [package insert]. U.S. Food and Drug Administration. Revised 2017. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761032lbl.pdf.
202. van der Heijde D, Klareskog L, Landewé R, Bruyn GA, Cantagrel A, Durez P, et al. Disease remission and sustained halting of radiographic progression with combination etanercept and methotrexate in patients with rheumatoid arthritis. Arthritis Rheum. 2007;56(12):3928-39. doi: 10.1002/art.23141. PubMed PMID: 18050208.
203. van der Heijde D, Klareskog L, Rodriguez-Valverde V, Codreanu C, Bolosiu H, Melo-Gomes J, et al. Comparison of etanercept and methotrexate, alone and combined, in the treatment of rheumatoid arthritis: two-year clinical and radiographic results from the TEMPO study, a double-blind, randomized trial. Arthritis Rheum. 2006;54(4):1063-74. doi: 10.1002/art.21655. PubMed PMID: 16572441.
204. van Vollenhoven RF, Ostergaard M, Leirisalo-Repo M, Uhlig T, Jansson M, Larsson E, et al. Full dose, reduced dose or discontinuation of etanercept in rheumatoid arthritis. Ann Rheum Dis. 2016;75(1):52-8. Epub 20150414. doi: 10.1136/annrheumdis-2014-205726. PubMed PMID: 25873634; PubMed Central PMCID: PMC4717401.
205. Volansky R. Golden age of rheumatology: Comparing drug-associated risk in pre-biologic era vs. today. Healio Rheumatology [Internet]. 2022. Available from: https://www.healio.com/news/rheumatology/20220610/golden-age-of-rheumatology-comparing-drugassociated-risk-in-prebiologic-era-vs-today.
206. Wang R, Dasgupta A, Ward MM. Comparative Efficacy of Tumor Necrosis Factor-α Inhibitors in Ankylosing Spondylitis: A Systematic Review and Bayesian Network Metaanalysis. J Rheumatol. 2018;45(4):481-90. Epub 20180115. doi: 10.3899/jrheum.170224. PubMed PMID: 29335342.
207. Wang SH, Yu CL, Wang TY, Yang CH, Chi CC. Biologic Disease-Modifying Antirheumatic Drugs for Preventing Radiographic Progression in Psoriatic Arthritis: A Systematic Review and Network Meta-Analysis. Pharmaceutics. 2022;14(10). Epub 20221008. doi: 10.3390/pharmaceutics14102140. PubMed PMID: 36297574; PubMed Central PMCID: PMC9608970.
208. Ward MM, Deodhar A, Gensler LS, Dubreuil M, Yu D, Khan MA, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Nonradiographic Axial Spondyloarthritis. Arthritis Care Res (Hoboken). 2019;71(10):1285-99. Epub 20190821. doi: 10.1002/acr.24025. PubMed PMID: 31436026; PubMed Central PMCID: PMC6764857.
209. Weinblatt ME, Bathon JM, Kremer JM, Fleischmann RM, Schiff MH, Martin RW, et al. Safety and efficacy of etanercept beyond 10 years of therapy in North American patients with early and longstanding rheumatoid arthritis. Arthritis Care Res (Hoboken). 2011;63(3):373-82. Epub 20101018. doi: 10.1002/acr.20372. PubMed PMID: 20957659.
210. Weinblatt ME, Kremer JM, Bankhurst AD, Bulpitt KJ, Fleischmann RM, Fox RI, et al. A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. N Engl J Med. 1999;340(4):253-9. doi: 10.1056/nejm199901283400401. PubMed PMID: 9920948.

211. Whitlock SM, Enos CW, Armstrong AW, Gottlieb A, Langley RG, Lebwohl M, et al. Management of psoriasis in patients with inflammatory bowel disease: From the Medical Board of the National Psoriasis Foundation. J Am Acad Dermatol. 2018;78(2):383-94. doi: 10.1016/j.jaad.2017.06.043. PubMed PMID: 29332708.
212. Wu E, Chen L, Birnbaum H, Yang E, Cifaldi M. Retrospective claims data analysis of dosage adjustment patterns of TNF antagonists among patients with rheumatoid arthritis. Curr Med Res Opin. 2008;24(8):2229-40. Epub 20080623. doi: 10.1185/03007990802229548. PubMed PMID: 18577308.
213. Wu JJ. Contemporary management of moderate to severe plaque psoriasis. Am J Manag Care. 2017;23(21 Suppl):S403-s16. PubMed PMID: 29297664.
214. Wu N, Bhurke S, Shah N, Harrison DJ. Application of a validated algorithm to estimate the effectiveness and cost of biologics for rheumatoid arthritis in the US pharmacy benefit manager context. Clinicoecon Outcomes Res. 2015;7:257-66. Epub 20150513. doi: 10.2147/CEOR.S83932. PubMed PMID: 25999750; PubMed Central PMCID: PMC4435053.
215. Xie F, Yun H, Bernatsky S, Curtis JR. Brief Report: Risk of Gastrointestinal Perforation Among Rheumatoid Arthritis Patients Receiving Tofacitinib, Tocilizumab, or Other Biologic Treatments. Arthritis Rheumatol. 2016;68(11):2612-7. doi: 10.1002/art.39761. PubMed PMID: 27213279; PubMed Central PMCID: PMC5538140.
216. Yip K, Navarro-Millán I. Racial, ethnic, and healthcare disparities in rheumatoid arthritis. Curr Opin Rheumatol. 2021;33(2):117-21. doi: 10.1097/bor.0000000000000782. PubMed PMID: 33394602; PubMed Central PMCID: PMC8009304.
217. Ytterberg SR, Bhatt DL, Mikuls TR, Koch GG, Fleischmann R, Rivas JL, et al. Cardiovascular and Cancer Risk with Tofacitinib in Rheumatoid Arthritis. N Engl J Med. 2022;386(4):316-26. doi: 10.1056/NEJMoa2109927. PubMed PMID: 35081280.
218. Yun H, Xie F, Delzell E, Chen L, Levitan EB, Lewis JD, et al. Risks of herpes zoster in patients with rheumatoid arthritis according to biologic disease-modifying therapy. Arthritis Care Res (Hoboken). 2015;67(5):731-6. doi: 10.1002/acr.22470. PubMed PMID: 25201241; PubMed Central PMCID: PMC5765980.
219. Yun H, Xie F, Delzell E, Chen L, Yang S, Saag KG, et al. The comparative effectiveness of biologics among older adults and disabled rheumatoid arthritis patients in the Medicare population. Br J Clin Pharmacol. 2015;80(6):1447-57. Epub 20150930. doi: 10.1111/bcp.12709. PubMed PMID: 26130274; PubMed Central PMCID: PMC4693474.
220. Závada J, Lunt M, Davies R, Low AS, Mercer LK, Galloway JB, et al. The risk of gastrointestinal perforations in patients with rheumatoid arthritis treated with anti-TNF therapy: results from the BSRBR-RA. Ann Rheum Dis. 2014;73(1):252-5. Epub 20130505. doi: 10.1136/annrheumdis-2012-203102. PubMed PMID: 23644671.
221. Zisman D, Bitterman H, Shalom G, Feldhamer I, Comanesther D, Batat E, et al. Psoriatic arthritis treatment and the risk of herpes zoster. Ann Rheum Dis. 2016;75(1):131-5. Epub 20140926. doi: 10.1136/annrheumdis-2013-205148. PubMed PMID: 25261573.

Redacted Negotiation Meeting Summaries for Enbrel

Below are summaries of the negotiation meetings between CMS and the Primary Manufacturer, which include redacted information regarding the negotiation meetings and exchange of offers and counteroffers in the meetings.

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Washington, DC 20201

SUBJECT: Meeting Summary from Negotiation Meeting between the Centers for Medicare & Medicaid Services (CMS) and Immunex Corporation regarding Enbrel on May 2, 2024

Background: Sections 11001 and 11002 of the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169), signed into law on August 16, 2022, established the Medicare Drug Price Negotiation Program (hereafter the "Negotiation Program") to enable the Centers for Medicare & Medicaid Services (CMS) to negotiate maximum fair prices (MFPs) with willing manufacturers for certain high expenditure, single source drugs and biological products. Immunex Corporation (hereafter "the Primary Manufacturer") chose to enter into an agreement to participate in the Negotiation Program for Enbrel (hereafter "the Selected Drug").

In accordance with revised guidance and in the course of negotiation for the Selected Drug, CMS invited the Primary Manufacturer to a negotiation meeting when rejecting the Primary Manufacturer's counteroffer, and the Primary Manufacturer accepted CMS' invitation. CMS shared a proposed meeting agenda with the Primary Manufacturer approximately two weeks before the meeting. The Primary Manufacturer had the opportunity to request additions or edits to the agenda at least one week ahead of the meeting. This document includes a summary prepared by CMS of the first negotiation meeting, which was held on May 2, 2024 between 1:00 PM ET and 3:30 PM ET.

CMS Attendees:

1. Kristie Gurley, Representative from the Office of the General Counsel
2. Dan Heider, Director, Division of Rebate Agreements and Drug Price Negotiation
3. Min Kwon, Division of Rebate Agreements and Drug Price Negotiation
4. Tina Li, Medicare Drug Rebate and Negotiations Group
5. Corey Rosenberg, Deputy Director, Division of Rebate Agreements and Drug Price Negotiation
6. Lara Strawbridge, Deputy Director of Policy, Medicare Drug Rebate and Negotiations Group

Primary Manufacturer Attendees:

1. William Connelly, Associate General Counsel
2. Gary Fanjiang, Vice President, U.S. Medical
3. Yola Gawlik, Executive Director, U.S. Health Policy and Reimbursement
4. Susan Logan, Vice President, General Manager Inflammation
5. Pallavi Rane, Senior Director Health Economics
6. David Zimmer, Vice President, U.S. Value & Access

Topics: The discussion focused on topics outlined in the final agenda for the meeting, which was as follows:[1]

- Introductions and meeting reminders
- Discussion of initial offer and any questions from the Primary Manufacturer
- Discussion of counteroffer and any questions from CMS
- Any other considerations that CMS and the Primary Manufacturer would like to discuss
- Next steps

[1] Note: This agenda may be inclusive of topics proposed by the Primary Manufacturer.

Offers/Counteroffers Exchanged:

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Washington, DC 20201

SUBJECT: Meeting Summary from Negotiation Meeting between the Centers for Medicare & Medicaid Services (CMS) and Immunex Corporation regarding Enbrel on May 23, 2024

Background: Sections 11001 and 11002 of the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169), signed into law on August 16, 2022, established the Medicare Drug Price Negotiation Program (hereafter the "Negotiation Program") to enable the Centers for Medicare & Medicaid Services (CMS) to negotiate maximum fair prices (MFPs) with willing manufacturers for certain high expenditure, single source drugs and biological products. Immunex Corporation (hereafter "the Primary Manufacturer") chose to enter into an agreement to participate in the Negotiation Program for Enbrel (hereafter "the Selected Drug").

In accordance with revised guidance and in the course of negotiation for the Selected Drug, because CMS and the Primary Manufacturer did not reach agreement on an MFP in the first negotiation meeting held on May 2, 2024, each party had the opportunity to request one additional negotiation meeting, resulting in a maximum of three meetings. CMS requested a second negotiation meeting and the Primary Manufacturer accepted the invitation. CMS shared a proposed meeting agenda with the Primary Manufacturer approximately two weeks before the meeting. The Primary Manufacturer had the opportunity to request additions or edits to the agenda at least one week ahead of the meeting. This document includes a summary prepared by CMS of the second negotiation meeting, which was held on May 23, 2024 between 10:00 AM ET and 12:30 PM ET.

CMS Attendees:

1. Kristie Gurley, Representative from the Office of the General Counsel
2. Dan Heider, Director, Division of Rebate Agreements and Drug Price Negotiation
3. Kaitlin Hunter, Division of Rebate Agreements and Drug Price Negotiation
4. Min Kwon, Division of Rebate Agreements and Drug Price Negotiation
5. Tina Li, Medicare Drug Rebate and Negotiations Group
6. Lara Strawbridge, Deputy Director of Policy, Medicare Drug Rebate and Negotiations Group

Primary Manufacturer Attendees:

1. William Connelly, Associate General Counsel (virtual attendance)
2. Gary Fanjiang, Vice President, U.S. Medical (virtual attendance)
3. Kelsey Lang, Executive Director, U.S. Health Policy and Reimbursement (virtual attendance)
4. Susan Logan, Vice President, General Manager Inflammation (virtual attendance)
5. Pallavi Rane, Senior Director Health Economics (virtual attendance)
6. David Zimmer, Vice President, U.S. Value & Access (virtual attendance)

Topics: The discussion focused on topics outlined in the final agenda for the meeting, which was as follows:[1]

- Introductions and meeting reminders
- Further discussion of real-world comparative evidence relative to therapeutic alternatives
- Any additional information from Primary Manufacturer on the impact of previously discussed access concerns
- Any other considerations that CMS or the Primary Manufacturer would like to discuss
- Next steps

[1] Note: This agenda may be inclusive of topics proposed by the Primary Manufacturer.

Offers/Counteroffers Exchanged:

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Medicare & Medicaid Services
200 Independence Avenue SW
Washington, DC 20201

SUBJECT: Meeting Summary from Negotiation Meeting between the Centers for Medicare & Medicaid Services (CMS) and Immunex Corporation regarding Enbrel on June 20, 2024

Background: Sections 11001 and 11002 of the Inflation Reduction Act of 2022 (IRA) (P.L. 117-169), signed into law on August 16, 2022, established the Medicare Drug Price Negotiation Program (hereafter the "Negotiation Program") to enable the Centers for Medicare & Medicaid Services (CMS) to negotiate maximum fair prices (MFPs) with willing manufacturers for certain high expenditure, single source drugs and biological products. Immunex Corporation (hereafter "the Primary Manufacturer") chose to enter into an agreement to participate in the Negotiation Program for Enbrel (hereafter "the Selected Drug").

In accordance with revised guidance and in the course of negotiation for the Selected Drug, because CMS and the Primary Manufacturer did not reach agreement on an MFP in the second negotiation meeting, which was requested by CMS and held on May 23, 2024, the Primary Manufacturer had the opportunity to request one additional negotiation meeting, resulting in a maximum of three meetings. The Primary Manufacturer requested a third negotiation meeting and CMS accepted the invitation. CMS shared a proposed meeting agenda with the Primary Manufacturer approximately two weeks before the meeting. The Primary Manufacturer had the opportunity to request additions or edits to the agenda at least one week ahead of the meeting. This document includes a summary prepared by CMS of the third negotiation meeting, which was held on June 20, 2024 between 10:00 AM ET and 12:30 PM ET.

CMS Attendees:

1. Kristie Gurley, Representative from the Office of the General Counsel (virtual attendance)
2. Dan Heider, Director, Division of Rebate Agreements and Drug Price Negotiation
3. Min Kwon, Division of Rebate Agreements and Drug Price Negotiation
4. Tina Li, Medicare Drug Rebate and Negotiations Group
5. Corey Rosenberg, Deputy Director, Division of Rebate Agreements and Drug Price Negotiation
6. Lara Strawbridge, Deputy Director of Policy, Medicare Drug Rebate and Negotiations Group

Primary Manufacturer Attendees:

1. William Connelly, Associate General Counsel (virtual attendance)
2. Gary Fanjiang, Vice President, U.S. Medical (virtual attendance)
3. Yola Gawlik, Executive Director, U.S. Health Policy and Reimbursement
4. Susan Logan, Vice President, General Manager Inflammation (virtual attendance)
5. Pallavi Rane, Senior Director Health Economics (virtual attendance)
6. David Zimmer, Vice President, U.S. Value & Access (virtual attendance)

Topics: The discussion focused on topics outlined in the final agenda for the meeting, which was as follows:[1]

- Introductions and meeting reminders
- Continued discussion of formulary access considerations
- Revised offer/counteroffer price discussion
- Any other considerations that CMS or the Primary Manufacturer would like to discuss
- Next steps

[1] Note: This agenda may be inclusive of topics proposed by the Primary Manufacturer.

Offers/Counteroffers Exchanged:

[redacted]

COLORADO
Prescription Drug Affordability Board
Division of Insurance

Prescription Drug Affordability Board DRAFT Meeting Minutes

Friday, December 8, 2023; 10 am - 2 pm - Virtual Meeting
Meeting Recording

Meeting Attendance

Board Members
Dr. Gail Mizner
Dr. Justin VandenBerg
Dr. Amy Gutierrez
Dr. Sami Diab
Ms. Cathy Harshbarger

Board Staff
Lila Cummings
Kate Davidson
Callie Shelton
Moroj Salih
Sagun Sharma
Abby Chestnut
Sara Stultz

Agenda

- Call to Order, Roll Call, Member Updates, Minutes Approval
- Board Business
- Break
- Director Updates
- Public Comment

Call to Order and Roll Call

Dr. Mizner called the meeting to order at 10:01 am and all Board members were present. No stakeholder meetings were disclosed by board members or staff members.

Approval of October 27 Meeting Minutes

Dr. Diab moved and Dr. VandenBerg seconded the motion to approve the October 27 meeting minutes. All Board members voted to approve the minutes.

DECISION: October 27 meeting minutes unanimously approved at 10:03 am.

Board Business

No conflicts of interest were declared by Board members for Trikafta. All Board members stated there was sufficient evidence to move ahead with deliberation concerning unaffordability of Trikafta. The Board moved to deliberation at 10:11 am and the Board staff director, Lila Cummings, began the presentation at 10:12 am. The Board deliberated the fifteen Affordability Review components and discussed information from the draft Affordability Review report.

Public Comment

Public comment regarding deliberations concerning unaffordability commenced at 11:27 am. The following individuals offered public comment to the Board:

COLORADO
Prescription Drug Affordability Board
Division of Insurance

- Bethany Pray
- Natalie Litton - Generation Patient
- Jamie Rubin-Cahill - Vertex
- Rose Keller
- Jen Reinhardt
- Laura Bonnell - Bonnell Foundations
- Scott Bertani - Coalition of HealthHIV
- Kelly Wiberg
- Siri Vaeth - Director of CFRI
- Amanda Boone - CF United

Determination of Trikafta's Unaffordability
Motion for whether Trikafta is unaffordable began at 11:57 am. Dr. VandenBerg moved that the Board deem that use of Trikafta, consistent with the labeling approved by the FDA or standard medical practice, is not unaffordable for Colorado consumers. Dr. Diab seconded.
DECISION: The motion to deem Trikafta not unaffordable for Colorado consumers passed at 11:58. The Board unanimously voted in favor of Trikafta being not unaffordable. Trikafta is not eligible for a UPL.

Break

Dr. Mizner called for a 10 minute break from 12:01 to 12:11 pm.

Director Updates

The Board rescheduled the first meeting for 2024 on February 16. Staff gave recommendations for proposed changes on the following Rule and Policy:

- **Policy 04**: revision of timelines and methods of gathering patient and caregiver input
- **3 CCR 702-9 Rule Part 3**: proposed change that would allow the Board to consider a prescription drug's orphan drug status during the selection stage

Dr. Gutierrez proposed to put in Policy to revisit Affordability Reviews.

Board Business
The Board began Affordability Review data discussion for Genvoya at 12:21 pm. Dr. Diab disclosed a conflict of interest and recused. No other Board member disclosed any conflicts of interest. Lila Cummings presented the draft report results for Genvoya.

The Board began Affordability Review data discussion for Enbrel at 1:01 pm. Dr. Diab disclosed a conflict of interest and recused. No other Board member disclosed any conflicts of interest. Lila Cummings presented the draft report results for Enbrel.

Public Comment
The following individuals offered public comment to the Board starting at 1:35 pm**:**

COLORADO
Prescription Drug Affordability Board
Division of Insurance

- Michiel Peters - Global Coalition on Aging
- Lisbet Finseth - National MS Society
- Dan Scales - Director of Clinical Health
- Scott Bertani - HealthHIV
- Mannat Singh - Consumer Advocate CCHI
- Brett Johnson - AMGEN
- Janet Dorr
- Katelin Lucariello - Pharmaceutical Manufacturers of America

Dr. Mizner adjourned the meeting at 1:55 pm. The next PDAB meeting will be held on December 15, 2023 at 10 am MT, to adopt the final report for Trikafta.

COLORADO
Prescription Drug Affordability Board
Division of Insurance

Prescription Drug Affordability Board DRAFT Meeting Minutes
Friday, February 16, 2024; 1 - 5 pm - Virtual Meeting
Meeting Recording

Meeting Attendance

Board Members	**Board Staff**
Dr. Gail Mizner	Lila Cummings
Dr. Justin VandenBerg	Kate Davidson
Dr. Amy Gutierrez	Callie Shelton
Dr. Sami Diab	Moroj Salih
Ms. Cathy Harshbarger	Sagun Sharma
	Abby Chestnut
	Sara Stultz

Agenda

- Call to Order, Roll Call, Member Updates, Minutes Approval
- Opening Remarks
- Director Updates
- Board Business
- Break
- Board Business
- Public Comment

Call to Order and Roll Call
Dr. Mizner called the meeting to order at 1:01 pm and all Board members were present. Dr. Diab disclosed his meeting with Colorado Oncology Society, along with Board Director, Lila Cummings. Ms. Cummings also disclosed Board staff and DOI leadership's meeting with Gilead Sciences, Inc.

Approval of December 8 and December 15 Meeting Minutes
Dr. VandenBerg moved and Ms. Harshbarger seconded the motion to approve the December 8 meeting minutes. All Board members voted to approve the minutes.
DECISION: December 8 meeting minutes unanimously approved at 1:03 pm.
Dr. Diab moved and Dr. VandenBerg seconded the motion to approve the December 15 meeting minutes. All Board members, except Dr. Gutierrez, voted to approve the minutes. Dr. Gutierrez abstained, as she was not present at the December 15 meeting.
DECISION: December 15 meeting minutes unanimously approved at 1:05 pm.

Opening Remarks
Division of Insurance Commissioner Michael Conway made opening remarks at 1:06 pm.

Director Updates
Ms. Cummings, gave updates on PDAB-related bills in the 2024 Legislative Session. Additionally, Ms. Cummings updated the Board on proposed Affordability Review policy

changes, specifically considering orphan drug designation earlier in the process, alternative ways to engage patients and caregivers, and alternative ways to engage individuals with scientific and medical training. With respect to considering policy changes, the Board discussed Board staff engaging with stakeholders first, then bringing the feedback to the Board.

Executive Session
Ms. Harshbarger moved and Dr. Gutierrez seconded the motion to convene an executive session to receive legal advice from the Board's attorneys regarding responding to public comment about Genvoya pursuant to section 24-6-402(3)(a)(II), C.R.S. Dr. Diab disclosed a conflict of interest with both Enbrel and Genvoya. He voted for the Board to convene into an executive session, but recused himself from the session itself and did not attend.

DECISION: The Board voted unanimously to convene an executive session at 1:18 pm.

Executive session adjourned at 1:33 pm. The Board received legal advice from the Board's attorneys regarding responding to public comment about Genvoya. The Board did not conduct any Board business or deliberate any determination regarding Enbrel or Genvoya's unaffordability during the session.

Board Business

Conflicts of Interest Disclosures Regarding Enbrel and Genvoya: Dr. Diab disclosed a conflict of interest with Enbrel and Genvoya and recused himself from deliberation and votes relating to those drugs. No other Board member disclosed any conflicts of interest.

Enbrel Affordability Review Deliberation
All Board members stated there was sufficient evidence to deliberate concerning the unaffordability of Enbrel. The Board moved to deliberation at 1:35 pm, and Ms. Cummings began the presentation. The Board deliberated the fifteen Affordability Review components and discussed information from the draft Affordability Review report.

Public Comment
Public comment regarding Board deliberations concerning the unaffordability of Enbrel commenced at 3:00 pm. The following individuals/groups offered public comment to the Board:

- Tiffany Westrich-Robertson - AI Arthritis
- Brett Johnson - Amgen
- Hope Stonner - CCHI
- Steven Newmark - Global Healthy Living Foundation
- Jerry Cunningham
- Bridget Seritt

Determination of Enbrel's Unaffordability
At 3:18 pm, Ms. Harshbarger moved that the Board deem that use of Enbrel, consistent with the labeling approved by the FDA or standard medical practice, is unaffordable for Colorado consumers. Dr. Gutierrez seconded.

COLORADO
Prescription Drug Affordability Board
Division of Insurance

DECISION: The motion to deem Enbrel unaffordable for Colorado consumers passed at 3:22 pm. The Board unanimously voted in favor of Enbrel being unaffordable, except Dr. Diab who recused from the vote due to a conflict of interest with Enbrel. Enbrel is eligible for an Upper Payment Limit.

Break
Dr. Mizner called for a 15 minute break from 3:24 to 3:39 pm.
Board Business

Genvoya Affordability Review Deliberation
All Board members stated there was sufficient evidence to deliberate concerning the unaffordability of Genvoya. The Board moved to deliberation at 3:39 pm, and Ms. Cummings began the presentation. The Board deliberated the fifteen Affordability Review components and discussed information from the draft Affordability Review report.

Public Comment
Public comment regarding deliberations concerning the unaffordability of Genvoya commenced at 4:32 pm. The following individuals/groups offered public comment to the Board:

- Jen Laws - CANN SDAP
- Natalie Rose - Gilead
- Mark Thrun - Gilead
- Christopher Zivalich
- Michael Dorosh
- Scott Bertani - HealthHIV

Determination of Genvoya's Unaffordability
At 4:52pm, Dr. Gutierrez moved that the Board deem that use of Genvoya, consistent with the labeling approved by the FDA or standard medical practice, is not unaffordable for Colorado consumers. Dr. VandenBerg seconded.

DECISION: The motion to deem Genvoya not unaffordable for Colorado consumers passed at 4:53 pm. The Board unanimously voted in favor of Genvoya being not unaffordable, except Dr. Diab who recused from the vote due to a conflict of interest with Genvoya. Genvoya is not eligible for an Upper Payment Limit.

Public Comment
The following individuals offered general public comment to the Board starting at 4:54 pm**:**

- Amy Goodman - CO BioScience
- Mannat Singh - CCHI
- Katelin Lucariello - PhRMA
- Bridget Seritt

Dr. Mizner adjourned the meeting at 5:02 pm. The next PDAB meeting will be held on February 23, 2024 at 10:00 am MT, to adopt the final Affordability Review reports for Enbrel and Genvoya.

COLORADO
Prescription Drug Affordability Board
Division of Insurance

Prescription Drug Affordability Board DRAFT Meeting Minutes
Friday, February 23, 2024; 10 - 11 am - Virtual Meeting
Meeting Recording

Meeting Attendance

Board Members
Dr. Gail Mizner
Dr. Justin VandenBerg
Dr. Sami Diab
Dr. Amy Gutierrez

Board Staff
Lila Cummings
Kate Davidson
Callie Shelton
Moroj Salih
Sagun Sharma
Abby Chestnut
Sara Stultz

Absent
Ms. Cathy Harshbarger

Agenda
- Call to Order, Roll Call
- Board Business
- Public Comment

Call to Order and Roll Call
Dr. Mizner called the meeting to order at 10:10 am. All Board members were present, except Ms. Harshbarger.

Board Business
The Board voted on creating an ad hoc work group meeting in preparation for drafting the Board's General Assembly Report. Dr. Mizner and Dr. Gutierrez volunteered to run the work group meeting and help create the report. Dr. Diab motioned and Dr. VandenBerg seconded to create the ad hoc work group.

DECISION: The motion to create an ad hoc work group in preparation for the General Assembly Report passed unanimously at 10:20 am.

The Board discussed requesting additional information related to Cosentyx and Stelara at 10:24 am. Dr. Diab disclosed a conflict of interest with Cosentyx and recused himself from the discussion. No other Board member disclosed any conflicts of interest.

Board Director, Lila Cummings, presented the Board with the staff's plan to gather additional information on Cosentyx and Stelara from individuals with scientific and medical training, and patients and caregivers. Staff plans to re-open surveys and outreach to physicians and pharmacists actively prescribing and dispensing Cosentyx and Stelara. Dr. Mizner stated receiving feedback from a professional on the efficacy of the surveys before re-opening them

COLORADO
Prescription Drug Affordability Board
Division of Insurance

would be a good idea. Additionally, the Board discussed a preference for r medical professionals to disclose conflicts of interest when providing input in stakeholder meetings and surveys.

Executive Session

Dr. Mizner moved and Dr. Gutierrez seconded the motion to convene an executive session to receive legal advice from the Board's attorneys regarding public comments received on Enbrel pursuant to section 24-6-402(3)(a)(II), C.R.S. Dr. Diab disclosed a conflict of interest with Enbrel. He voted for the Board to convene into an executive session, but recused himself from the session itself and did not attend.

DECISION: The Board voted unanimously to convene an executive session at 10:29 am.

Executive session adjourned at 10:52 am. The Board received legal advice from the Board's attorneys regarding public comments received on Enbrel. The Board did not conduct any Board business or deliberate any determination regarding Enbrel's unaffordability during the session.

Board Business

The Board began the process of adopting the final Enbrel Affordability Review Report at 10:53 am. Dr. Diab disclosed a conflict of interest and recused. No other Board member disclosed any conflicts of interest. All Board members were present at the meeting on February 16, 2024 where it was determined that use of Enbrel, consistent with the labeling approved by the FDA or standard medical practice, is unaffordable for Colorado consumers.

No objections were made by Board members to move forward with adopting the final Enbrel Affordability Review Report. Board Staff presented proposed changes to the final affordability review report.. Dr. Gutierrez moved to approve the final Enbrel Affordability Review Report, and Dr. VandenBerg seconded.

DECISION: The motion to adopt the final Enbrel Affordability Review Report with the changes passed unanimously, except Dr. Diab who recused from the vote due to a conflict of interest with Enbrel. The final report was adopted at 10:55 am.

Public Comment

Public comment regarding deliberations concerning establishing an upper payment limit (UPL) for Enbrel commenced at 10:56 am. The following individuals/groups offered public comment to the Board:

- Tiffany Westrich-Robertson - AI Arthritis
- Brett Johnson - Amgen
- Corey Greenblat - Global Healthy Living Foundation
- Brian Warren - BIO
- Emily Zadvorny
- Hope Stonner - CCHI

COLORADO
Prescription Drug Affordability Board
Division of Insurance

Board Business

The Board voted on selecting Enbrel for establishment of a UPL. Dr. VandenBerg motioned and Dr. Gutierrez seconded that the Board select Enbrel for establishment of a UPL.

DECISION: The Board voted unanimously on selecting Enbrel for establishment of a UPL, except Dr. Diab who recused from the vote due to a conflict of interest with Enbrel, at 11:11 am.

The Board voted on directing Board staff to initiate rulemaking to establish a UPL for Enbrel. Dr. Gutierrez motioned and Dr. VandenBerg seconded.

DECISION: The Board voted unanimously on directing staff to initiate rulemaking to establish a UPL for Enbrel, except Dr. Diab who recused from the vote due to a conflict of interest with Enbrel, at 11:13 am.

The Board began the process of adopting the final Genvoya Affordability Review Report at 11:13 am. Dr. Diab disclosed a conflict of interest and recused. No other Board member disclosed any conflicts of interest. All Board members were present at the meeting on February 16, 2024 where it was determined that use of Genvoya, consistent with the labeling approved by the FDA or standard medical practice, is not unaffordable for Colorado consumers.

No objections were made by Board members to move forward with adopting the final Genvoya Affordability Review Report. Board Staff presented proposed changes to the final affordability review report. Dr. VandenBerg moved to approve the final Genvoya Affordability Review Report, and Dr. Gutierrez seconded.

DECISION: The motion to adopt the final Genvoya Affordability Review Report with the changes passed unanimously, except Dr. Diab who recused from the vote due to a conflict of interest with Genvoya. The final report was adopted at 11:14 am.

Ms. Cummings presented the Board with the proposed timeline for UPL Rulemaking. Dr. Mizner, Dr. Gutierrez, and Dr. VandenBerg discussed it is important to incorporate feedback and data, including public comment, during the UPL rulemaking process.

Dr. Mizner adjourned the meeting at 11:20 am. The next PDAB meeting will be held on March 15, 2024 at 10:00 am MT. The upcoming PDAAC meeting will be held on April 11, 2024 at 9:00 am MT.

Amgen Inc.
1 Amgen Center Drive
Thousand Oaks, CA 91320 USA
(805) 447-1000

amgen.com

December 5, 2023

Via email (*dora_ins_pdab@state.co.us*)

Colorado Department of Regulatory Agencies
Division of Insurance
ATTN: Dr. Gail Mizner, MD, FACP, AAHIVS, Chair, Colorado Prescription Drug Affordability Review Board (the "Board")
1560 Broadway, Suite 850
Denver, CO 80202

Re: ***Request for Immediate Attention on Two Critical Process Issues***

Dear Dr. Mizner:

On behalf of its wholly-owned subsidiary Immunex, Amgen respectfully calls the Board's attention to two issues arising out of its October 27, 2023 public meeting:

1. One Board member made on-the-record public comments about conversations with unnamed persons (in which Amgen was not involved) about Enbrel®'s affordability. Such information from a Board member may not be considered by the Board, whether offered in public or closed sessions.

2. Enbrel's affordability review data discussion was not afforded sufficient or equitable time.

Board Member Comment

During the meeting, while the Board was still discussing Trikafta, Board member Catherine Harshbarger offered a comment about unidentified people she stated she had "talked to personally," whom she described as having spent $6,000 out-of-pocket amount for Enbrel. ("Enbrel might be an example, where I've talked to people personally who've spent $6,000 out-of-pocket with their coinsurance.").

This is concerning. In previous public meetings, Ms. Harshbarger has not disclosed any independent engagements with Enbrel stakeholders, and Amgen is unaware of any that have been otherwise reported. In any event, Amgen believes such "ex parte" conversations by Board members must not be offered or taken into account by the Board. Any information considered by the Board should be subject to public comment, so the Board can make informed decisions based on accurate information. In this situation, Amgen is unaware of the source of the

information provided by Ms. Harshbarger, including critical details such as type of insurance, whether the patient was eligible for or enrolled in patient assistance programs, and over what period of time the patient paid out-of-pocket expenses. Therefore, we are unable to take a position as to whether the information she introduced is accurate. We accordingly request that the Board clarify that the statement made by Ms. Harshbarger will not be considered and state what evidence the Board believes it may consider (in both public and closed sessions), including but not limited to "off-the-record" discussions by members of issues before the Board. We also respectfully request that Ms. Harshbarger recuse herself from further Board deliberations related to Enbrel®, in order to ensure the integrity of the proceedings.

Discussion of Enbrel

According to the published agenda[1], the October 27, 2023 public meeting was to include "affordability review data discussions" for three drugs: Trikafta, Genvoya and Enbrel. While the Board devoted well over an hour to Trikafta, it allotted only 17 minutes of closed session discussion to Enbrel and Genvoya, combined. This was the case even though the Board acknowledged that Enbrel had more information to review than either Trikafta or Genvoya, which the Board attributed to the fact that Enbrel numerous FDA-approved indications.[2]

We also believe it is possible that Enbrel patients and members of the public may have been prevented from speaking during the "public comment" portion of the October 27 meeting. This worry arose after we learned that, even before the Board and staff announced they would only be discussing Enbrel in closed session, the link to sign up for public comment was no longer accepting responses. Indeed, no public commentators spoke about Enbrel specifically, which we believe may be attributed to the system not accepting their requests.

We understand the Board has since indicated that it plans to present draft affordability review results for Enbrel at its December 8, 2023 public meeting and to defer a vote on Enbrel until February 2, 2024. Because the vote on affordability for Trikafta is also scheduled to occur at the December 8 meeting, and, in light of how the Board's public discussion time was allocated on October 27, we are concerned this still may not provide a fair and equitable opportunity for Enbrel's affordability discussion.

While we understand the Board may elect to meet in certain closed sessions prior to February, we do not believe such private meetings are an adequate substitute for the opportunity to speak that a public session provides to Enbrel patients, the public, and Amgen. Indeed, we note that

[1] *See* October 27, 2023 Meeting Agenda, available online at https://doi.colorado.gov/insurance-products/health-insurance/prescription-drug-affordability-review-board.

[2] "And as you'll see in coming slides, we learned quite quickly that if there's a prescription drug that treats multiple indications, just the volume of research that's involved can be more. And so for Trikafta and Genvoya, since they only treat one indication, the research is a little more efficient in compiling for you all." October 27 Meeting, available online at https://us06web.zoom.us/rec/play/JehJBAfQP4Ew-YsDepUKS1nj1zb2K3qrYeAaJZ6GY8ID8lSr20wjaoNhoXI54oLmEJ9A_sBBerz9eiMs.CSCLX0hrX1V3uSSe?canPlayFromShare=true&from=share_recording_detail&continueMode=true&componentName=rec-play&originRequestUrl=https%3A%2F%2Fus06web.zoom.us%2Frec%2Fshare%2FtEwiigKuEEUIKxhuQ_ZEVd_HDI7bw1ZLUeZKOzXhmEEeSU4dyHU1I950XYhIkvhQ.iWoSl8S4blBjiB_k.

multiple times during the October 27 meeting, PDAB staff stated that the *public* discussion helped them understand the affordability factors. In fact, during the meeting, Board members and staff were able to talk through certain unclear and potentially inaccurate information about the drug they discussed. Enbrel has not had this opportunity.

Such a public discussion is clearly warranted, as several points in the October 27, 2023 Board deck require clarification and/or correction. For example, Slide 83 references input from different categories of healthcare professionals but does not attribute the included quotation and there has been no opportunity to ask questions about what different views the queried groups had. Slides 84 and 86 mistakenly reference Trikafta and not Enbrel (though both were included in the Enbrel section of the deck). And, even beyond these errors, there are issues that would clearly benefit from public discussion. Slides 93 and 94, for example, address prices' effect on Enbrel access, non-adherence, and utilization. An open discussion about these issues, including the opportunity for patients and the public to comment, would assist the Board in defining its perspective on insurer and PBM behavior. This is particularly important for Enbrel, a drug that treats multiple indications and has several therapeutic alternatives.

We thus believe a public discussion—allotting fair time to Enbrel and providing clarity and direction on the points set out above and related issues—should take place *before* any determination, draft or final, regarding affordability.

* * *

In closing, we reiterate that Amgen is driven by its mission to serve patients and committed to improving lives by discovering and developing treatments and cures for serious diseases. Amgen understands that the cost of prescription drugs is a concern for many Coloradans. We look forward to the opportunity to hear fair and open Board discussion about affordability of and access to Enbrel®, and we thank you for your careful attention to these issues.

Regards,

/s/ Kathy Sherman

Kathy Sherman
Associate Vice President, State and International Government Affairs
Global Government Affairs & Policy

Amgen Inc.
1 Amgen Center Drive
Thousand Oaks, CA 91320 USA
(805) 447-1000

amgen.com

February 1, 2024

Via email (*dora_ins_pdab@state.co.us***)**

Colorado Department of Regulatory Agencies, Division of Insurance
ATTN: Dr. Gail Mizner, MD, FACP, AAHIVS, Chair, Colorado Prescription Drug Affordability Review Board (the "Board")
1560 Broadway, Suite 850
Denver, CO 80202

Re: ***Request for Board Attention to Persistent Process Issues in Advance of Enbrel® Report Review and Votes***

Dear Dr. Mizner:

On behalf of Amgen and its wholly-owned subsidiary, Immunex, we direct the Board's attention to several issues, two of which were previously brought to your attention in Amgen's December 5, 2023 letter. These issues raise serious concerns about the fairness and legality of the Board's review process. We request that these issues be addressed before the Board takes any vote related to Enbrel®:

1. During the October 27, 2023 and December 8, 2023 public meetings, one Board member made on-the-record public comments about conversations with unnamed persons (in which Amgen was not involved) about Enbrel®'s affordability. Such information from a Board member may not be considered by the Board, whether offered in public or closed sessions.

2. The Board has been inconsistent with respect to the standards and procedures it is applying, and the opportunities to assess the information before the Board and meaningfully respond are inadequate and inconsistent with Board policy and stated principles.

Board Member Comments

During the October 27, 2023 meeting, while the Board was still discussing Trikafta, Board member Catherine Harshbarger made comments about unidentified people she stated she had "talked to personally," whom she described as having spent $6,000 out-of-pocket for Enbrel ("Enbrel might be an example, where I've talked to people personally who've spent $6,000 out-of-pocket with their coinsurance."). We raised this issue to you in our December 2, 2023 letter. At the December 8, 2023 meeting, despite our letter identifying the previous comments as a significant process issue, Ms. Harshbarger again cited off-the-record discussions, but the purported figure had grown by 25 percent to $8,000 ("I've talked to people that are spending as much as $8,000 out of their own pocket for Enbrel.").

Case 1:25-cv-3452-DDD-STV

Exhibit 49

These remarks, and that they remain unaddressed, contribute to our growing concerns about the lack of standards that are governing the Board's decision-making process and the inconsistent and inadequate processes followed by the Board. In previous public meetings, Ms. Harshbarger has not disclosed any independent engagements with Enbrel® stakeholders, and Amgen is unaware of any that have been otherwise reported. In any event, Amgen believes it is improper for Board members to engage in, or to consider, such "ex parte" conversations. Any information considered by the Board should be submitted publicly and on the record so that Amgen and other interested parties can have a meaningful opportunity to respond, the Board can make informed decisions based on accurate and complete information, and to ensure that there is appropriate accountability for the Board's decisions and actions.

Amgen remains unaware of the source of the information provided by Ms. Harshbarger at either meeting, including whether the conversations were with the same people (and, if not, which price figure she intended to communicate), critical details concerning the type of insurance, whether the patient or patients were eligible for or enrolled in patient assistance programs, and over what period of time the patient(s) paid out-of-pocket expenses. We are therefore unable to comment on and respond meaningfully to the information she introduced. We accordingly request that the Board clarify that the statement made by Ms. Harshbarger will not be considered and state what evidence the Board believes it may consider (in both public and closed sessions), including but not limited to "off-the-record" discussions by members concerning issues before the Board. We also request that Ms. Harshbarger provide in detail the basis for the information she stated on the record and that the Board provide an opportunity for public comment. Failing those steps, and in light of her improper ex parte research and the apparent bias reflected in her statements, we respectfully submit that Ms. Harshbarger should recuse herself from Board deliberations related to Enbrel®, in order to ensure the integrity of the proceedings.

Inadequate Opportunity to Assess and Meaningfully Respond to Information

It is essential that the Board adopt consistent standards and follow consistent procedures. While we recognize that the Board's delay of the Enbrel® affordability report review from December 8, 2023 to February 16, 2024 allowed for a discussion of preliminary information at the December 8 meeting, the time afforded for discussion of Enbrel® remains inadequate and has not been comparable to that afforded to Trikafta. At the October 27 meeting, the Board devoted well over an hour to Trikafta but allotted only 17 minutes of closed session discussion to Enbrel® and Genvoya, combined. At the December 8 meeting, the Board discussed Enbrel® for approximately half an hour in open session. The information before the Board, however, was unclear (e.g., references to Trikafta in the Enbrel slides and no specified time period from which the data were compiled) or incomplete (e.g., data not provided on many of the slides). Moreover, unlike the Trikafta presentation, the presentation from the December 8 meeting has still not been publicly posted, much less updated, on the Board's website as of February 1.

We are also concerned that Enbrel® patients and members of the public may have been prevented from speaking during the "public comment" portion of the October 27 meeting, and no one was permitted to make public comment during the December 15 meeting. First, we learned that, even

before the Board and staff announced they would only be discussing Enbrel® in closed session, the link to sign up for public comment was no longer accepting responses, and no public commenters spoke about Enbrel® specifically. Second, the lack of any opportunity for public comment at the December 15 meeting was contrary to the Board's Policy #2, entitled *Policies and Procedures required by § 24-3.7-102, C.R.S.*, which states, "The Board will provide the opportunity for public comment at each meeting." Amgen, and potentially other stakeholders, had questions and comments regarding the Board's standards and the means by which they were applied to the vote on whether Trikafta was unaffordable to Colorado consumers. Amgen and others have been harmed by not being afforded a reasonable opportunity to raise these issues in the public meeting.

We understand the Board may elect to meet in certain closed sessions, but such meetings obviously do not provide an opportunity for Enbrel® patients, the public, and Amgen to address the Board, making the lack of opportunity at public meetings all the more problematic. Additionally, while the Board and staff have stated on occasion that comments may be submitted in writing, those comments have so far not been acknowledged or responded to. The Board is obliged to respond meaningfully to comments and to ensure that it takes into account the important information that public comment can provide.

We remain concerned that Amgen has been deprived of any meaningful opportunity to address or respond to the information before the Board. Indeed, the deadline for the sole confidential, drug-specific submission requested from manufacturers occurred prior to any clarity being provided on the information that would form the basis of the affordability determination. For instance, the key data populating the *Colorado PDAB 2023 Eligible Drug Dashboard* is identified as 2021 data, yet many of the key figures cited in the Trikafta affordability report are identified as 2022 data. Because we have not been afforded the opportunity to review any 2022 data from the Colorado All-Payer Claims Database (APCD) or the newly reported "top 15" drug lists from payers and pharmacy benefit managers (PBMs), we are unable to provide information that places such data in appropriate context or otherwise clarifies or responds to the information before the Board.

Furthermore, with the Board's reopening of the window for certain stakeholder input through January 21, 2024 and little, if any, information provided on the stakeholders targeted for that additional input, we lack insight into the current state of such information or the impartiality of the process, as we understood was an intent for the public nature of the previous stakeholder listening sessions. These irregularities contribute to our substantial concerns about the introduction of bias from the Board's and staff's selective targeting of stakeholders for input.

We thus believe a public discussion—allotting fair time to Enbrel® and providing clarity and direction on the points set out above and related issues—should take place *before* any determination, draft or final, is made regarding affordability.

* * *

Amgen is driven by its mission to serve patients and committed to improving lives by discovering and developing treatments and cures for serious diseases. Amgen understands that the cost of prescription drugs is a concern for many Coloradans, but also recognizes that these concerns will

only increase if the Board fails to comply with proper procedures and fails to allow for proper public comment. We look forward to the opportunity to hear fair and open Board discussion about affordability of and access to Enbrel®, and we thank you for your attention to these issues.

Regards,

/s/ Kathy Sherman

Kathy Sherman
Associate Vice President, State and International Government Affairs
Global Government Affairs & Policy