

# Biologics: A Different Class Of Medications That Makes A Difference For Our Patients

## *Information From The National Physicians Biologics Working Group*

As physicians, we see the influence of biological products firsthand. Our patients who would formerly have been confined to wheelchairs now continue to walk 25 years after being diagnosed with multiple sclerosis. Uncontrollable muscle contractions can be quieted, dangerously low white blood cell counts reversed, and some deadly cancers driven into remission. In many areas of medicine, biological products have had a substantial impact on our patients' lives—not just the modest increments we have seen from so many treatments in the past, but meaningful, game-changing improvements. In some cases, biological products treat serious medical conditions for which no other therapies are available.<sup>1</sup>

Biological products, also known as biologics, are made by cells or living organisms and are used for the prevention or treatment of disease. These therapies take many forms, including living cells, tissues, genes delivered in viruses, and proteins such as antibodies, growth factors, and enzymes.<sup>1</sup> Vaccines are familiar preventive biologics, whereas blood and blood products are familiar therapeutic biologics.



*“Before the advent of biologics, my patients with multiple sclerosis faced relentless physical deterioration and death. Biological therapies have turned this formidable disease into a manageable, chronic condition for many.”*

**David Charles, M.D.**  
Neurologist

## Examples Of Biological Therapies

Some examples of biological products and the conditions they are used to treat are listed in the following table. As shown here, biologics span many different areas of medicine, including neurology, oncology, hematology, dermatology, rheumatology, and oral surgery.

Biologic Therapy	Illness Or Condition Treated
Monoclonal Antibodies	Breast cancer <sup>a</sup> Arthritis <sup>b</sup> Psoriasis <sup>c</sup> Inflammatory bowel disease
Cytokines and growth factors	Multiple sclerosis <sup>d</sup> Foot ulcers in diabetics <sup>e</sup> Chemotherapy complications <sup>f</sup>
Botulinum neurotoxins	Spasticity and overactive muscle conditions <sup>g</sup> Chronic migraine <sup>h</sup>
Tissue Replacement Therapies	Burns and wounds

a. HER2/neu receptor monoclonal antibody for HER2 positive breast cancer

b. Tumor necrosis factor- $\alpha$  blockers (receptor antagonists and antibodies) for rheumatoid arthritis

c. Tumor necrosis factor- $\alpha$  blockers (receptor antagonists and antibodies) for psoriasis

d. Interferons for multiple sclerosis

e. Topical platelet-derived growth factor for diabetic foot ulcers

f. Granulocyte colony stimulating factors for chemotherapy-induced neutropenia or erythropoietins for anemia

g. Botulinum neurotoxins for focal upper-limb spasticity and focal dystonias such as cervical dystonia and blepharospasm

h. OnabotulinumtoxinA for chronic migraine

## *Differences Between Biologics And Conventional Drugs*

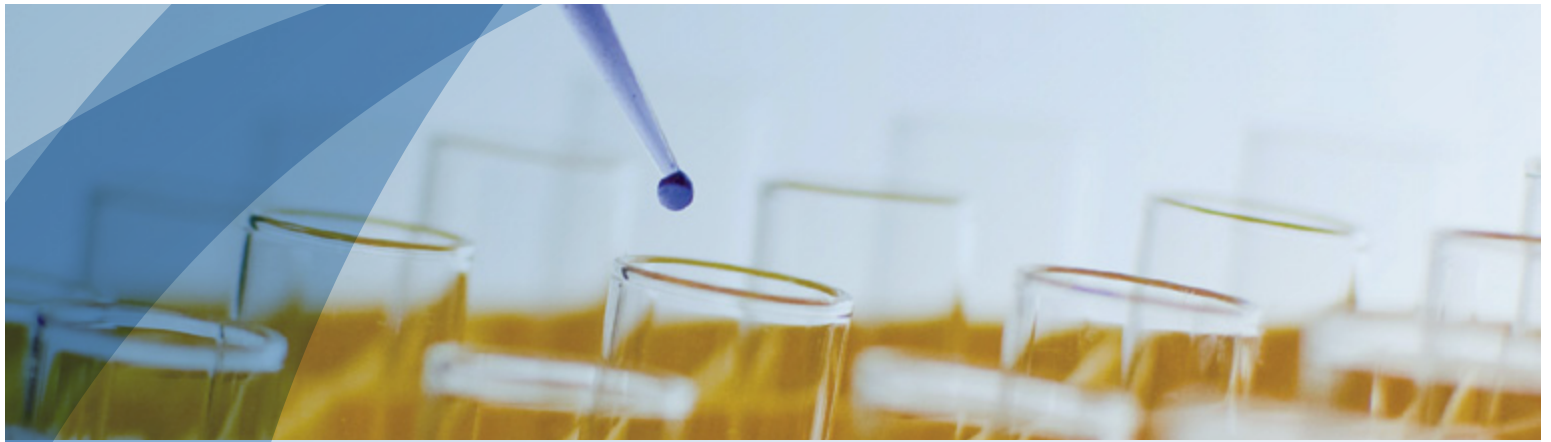
What makes biological products different from conventional drugs like aspirin, codeine, diazepam, and the statins? The most obvious difference is that biologics are made by cells or living organisms, whereas conventional drugs are synthesized in the laboratory using a series of known chemical reactions. Biologically synthesized products tend to be much more complex than chemically synthesized drugs and are more difficult to analyze.<sup>2</sup> In some cases, current technologies are not adequate to fully characterize the content of a given biological product—many of which contain more than one component. Additionally, the doses of many biologics are measured by their activity instead of by their weight, as is typical for conventional drugs whose doses are usually measured in milligrams.

Given that some of our most important current biological products are proteins, it is worth considering the unique features of these therapies. Proteins tend to be 100 to 1000 times larger than conventional drugs, and are more susceptible to physical factors such as light, heat, and agitation. In addition to their primary structures, or the amino acids chemically strung together in specific sequences, proteins also have secondary, tertiary, and even quaternary structures. These structures are characterized by specific twists, folds, bends, and chemical associations that are typically essential to the protein's activity. Even minor changes in these characteristics can affect how protein therapies perform in humans.<sup>2</sup>



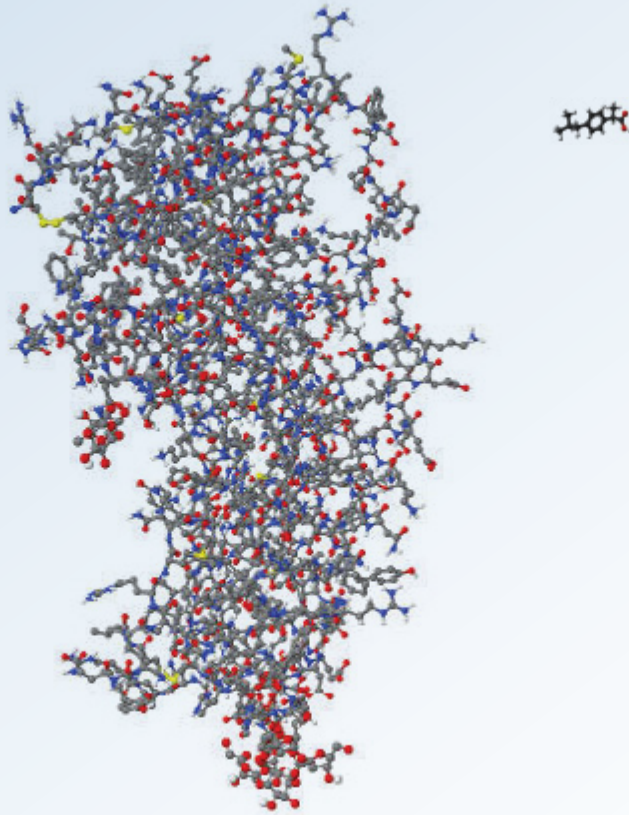
*“In the last ten years we have seen a dramatic difference in the control of autoimmune disorders, rheumatoid arthritis in particular. This crippling arthritis has been “tamed” in many patients with the use of newer biologics. Access to these expensive medicines is rapidly becoming the new challenge.”*

**Rudy Molina, M.D.**  
Rheumatologist



**Biological Protein Product**

**Ibuprofen**



Protein structure from RCSB Protein Data Bank, Identifier #1AU1

***The graphic above shows the vast differences in size and structural complexity between a conventional drug, ibuprofen, and a biological product.***

Another important aspect of proteins is their potential to stimulate immune responses. Seemingly inconsequential changes to the manufacture or production of protein therapies can lead to immune consequences in patients.<sup>3</sup> The extreme sensitivity of biological products to their manufacturing methods has led to a different set of regulations than for conventional drugs. Every step in the production of these medicines must be scrutinized in a way that is not necessary for chemically synthesized compounds.

## Challenges For Biologics

As you might imagine, the complexity that gives biologics their unique nature can also confer challenges. Here we consider three salient issues with biologics that are important to us as physicians.

### **Patient Expense**

Biological products can be extremely costly for patients to afford even with assistance programs. At least part of this expense can be attributed to the complexities inherent in developing suitable manufacturing processes for these therapies, which typically require elaborate and highly technical procedures owing to their biological nature.

Today, our country is at a crossroads in healthcare. We face unprecedented debt and unsustainable healthcare expenses. As legislators scrutinize the budget, deciding what can and cannot be cut, it is important not to lose sight of a fundamental point of agreement—providing the best possible treatments for patients who need them. Such treatments are increasingly biological products. For this reason, we must overcome the cost challenges associated with biologics.

With any purchase, an important aspect in weighing cost is value— the “bang for your buck.” None of us relishes paying an initially high price for something with the understanding that it will be more beneficial to us, and perhaps even save us money, in the long run. However, biological products often do just that. In some cases, biological products can reduce hospitalization,<sup>4</sup> disease relapses,<sup>5</sup> and even deaths.<sup>6</sup> Patients with some conditions show increased employment<sup>7</sup> or a return to normal physical functioning.<sup>8</sup> These benefits may help offset the initial purchase price of biologics and lead to eventual cost savings. In addition are the intangible benefits to our patients such as the improved quality of life.<sup>9, 10</sup> This is not to say that every patient who is treated with a biologic for a given condition will realize these benefits. Rather, it is to recognize that, as a group, biologics are transformative therapies for a number of serious medical conditions and their initial purchase price simply does not reflect their true comparative value.



*“An effective biologic can change the course of a disease. With the aid of biologics, we have made significant strides in improving survival from cancer.”*

**Emily Chan, M.D., PhD**  
Medical Oncologist



### **Patient Safety**

Another important challenge with biological products is ensuring patient safety. We have already seen how manufacturing processes for these medications are more complex than those of conventional drugs. Small changes in the way these medicines are produced can lead to unforeseen safety issues.<sup>3</sup> Similarly, when comparing one biological product to another, the test of pharmacologic bioequivalence—the standard procedure used to compare conventional drugs—is not relevant.<sup>11</sup> Instead, clinical testing is required for each individual biological product, even if it contains the same biologically active component(s) as a product that is already on the market.

### **Need To Preserve Physician Decision Making**

A third challenge with biologics is the need to preserve physician decision making in the current climate of healthcare reform. That is, insurers or other third parties should not be allowed to dictate what therapies physicians can prescribe and patients can access. The choice and the responsibility of prescribing biologics should reside with physicians. Physicians, not insurance companies or other third parties, have the medical education necessary to safely prescribe these powerful therapies based on knowledge of each patient's unique medical history.

### **Conclusion**

As physicians, we recognize that biological products often represent the cutting edge of healthcare, providing benefits to our patients not achievable with conventional drugs. We want patients to be able to afford these therapies and urge policy makers to work toward that goal. Affordability, however, cannot come at the expense of safety. Producing these medications is not a simple reaction that any well-trained chemist can carry out. Each step of the manufacturing process must be carefully developed and monitored, and the final product quality controlled and verified in clinical trials. This type of caution costs money and thus safety must be balanced with the need for patient access. Finally, we believe that the decision to prescribe a biological therapy, as well as the specific nature of that therapy, should rest with physicians. With these objectives in mind, we support the development of a policy toward biological products that balances patient affordability with safety and physician autonomy.



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The National Physicians Biologics Working Group is a project of the Alliance for Patient Access

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