

Biologics:

Can Patients Get What The Doctor Orders?

Challenges With Patient Access To Biological Medications Under The Current Healthcare Benefits Design

Information From The National Physicians Biologics Working Group

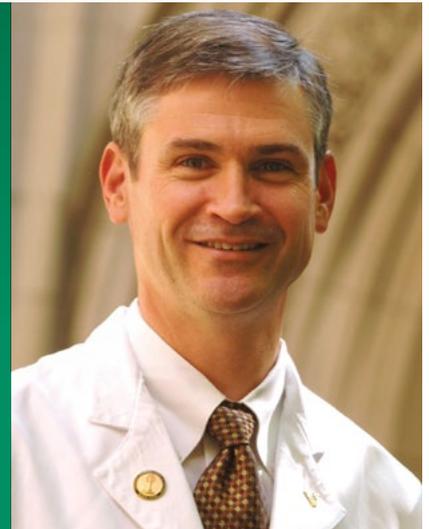
What if you had a chronic disease causing increasing disability whose progression could be slowed by a medication that you could not afford? Or, what if your physician prescribed a certain medication that your insurance company elected not to cover? What if your insurance company refused to pay for the medication until you suffered through a cheaper treatment they insisted upon, only to find that it failed to control your symptoms and your condition worsened? Unfortunately, these situations are all too common when patients try to obtain a class of therapies known as biologics.

As physicians, we want to provide our patients with the best possible care. For many chronic diseases of the immune system, joints, nervous system, skin, and even for cancer, this increasingly means treating patients with biological products. 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 proteins, living cells, tissues, and genes delivered in viruses.¹

A previous document from the National Physicians Biologics Working Group entitled *Biologics: A Different Class of Medications That Makes a Difference for Our Patients* described some of the major differences between biologics and conventional drugs, as well as some of the challenges that arise from these differences (available at: www.biologicsdoc.org). Here we extend our discussion by considering how insurance benefit structures developed for conventional drugs can interfere with the ability of our patients to obtain biologics. This discussion is critical because, for many chronic diseases, biologics produce meaningful reductions in disease progression and symptoms that cannot be obtained with conventional drugs.

“At a time of tremendous medical progress in the development of biologics to combat some of the most disabling diseases, too many patients face extreme challenges in gaining access to these remarkable life-saving therapies”.

David Charles, M.D.
Neurologist



“Fail First” Policies

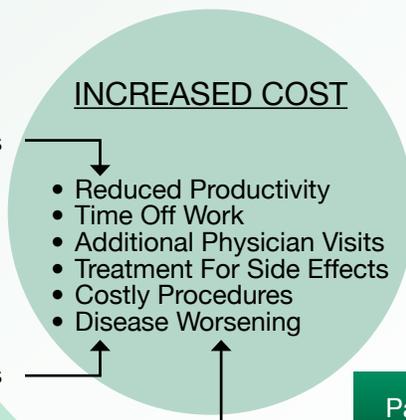
A common feature of healthcare benefit plans is a policy known as “fail first.” Under this policy, patients must first try the lowest-cost medication for their disease, then proceed to higher-cost medications in a stepwise fashion if the first medication is inadequate or intolerable.

When viewed solely from a medication cost perspective, the fail first policy seems to make sense. Why choose a more expensive medication when a less costly one will do? The problem is that, for many patients, the less expensive medication will not “do.” As physicians, we select the best medication for each of our patients by taking into consideration not only the disease, but also our individual patient’s medical history, likelihood of specific side effects, ability to tolerate particular side effects, and quality of life concerns. In this way, we try to match the patient to the treatment. Often a medication that works well for one patient will cause unacceptable side effects in another. The second patient may experience needless anxiety and suffering that could have been avoided if the physician—not the insurance company—were allowed to select the medication.

In addition to these humanistic concerns, it is also important to examine the larger economic consequences of fail first policies, which are referred to by insurers as stepped therapy. Stepped therapy is cost effective if a patient’s condition is controlled by the first medication. However, if the medication fails to control the disease, patients may miss work or experience dramatically reduced productivity, and may seek help at an emergency department or, at the least, must return to the physician’s office for another visit to change their medication. Such visits may entail costly procedures such as computerized tomography (CT) or magnetic resonance imaging (MRI). The following graphic shows how these costs accumulate.

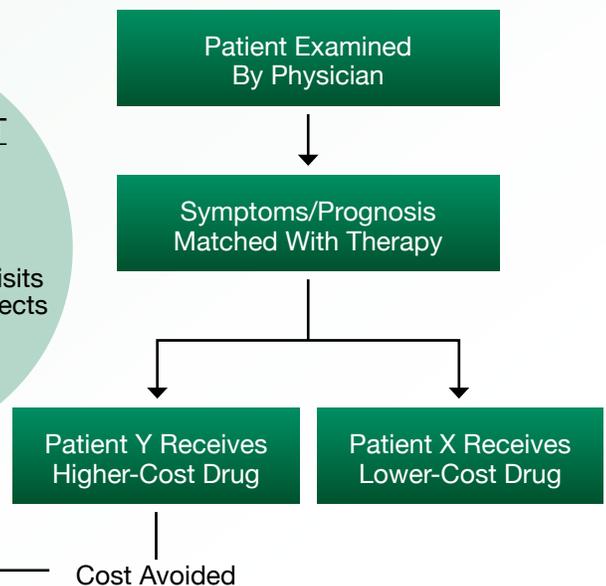
Example Of Stepped Vs. Segmented Approach To Therapy Showing Potential Sources Of Additional Costs Incurred At Each Step

STEPPED THERAPY



SEGMENTED THERAPY

(also referred to as INDIVIDUALIZED or PERSONALIZED)



Pay Now Or Pay Later?

Unfortunately, many insurers may not view this entire picture due to the division of insurance policies into pharmacy benefits and medical benefits. The pharmacy insurers are concerned only with minimizing medication costs even if it means higher medical costs in the future because the latter do not come out of their budgets.

In the case of biologics, the fail first policy takes on added urgency because the conditions they are used to treat are typically chronic and incurable, often progressive, and not infrequently deadly. For many of these diseases, biologics are used not only to control symptoms, but also to prevent the patient's condition from worsening and to minimize progression to comorbid states such as an increase in cardiovascular events.

Also, like all medications, biologics can have side effects. It is important to consider each patient's medical history and ability to tolerate the particular side effects associated with each biologic before prescribing that therapy. In other words, starting a patient on a biologic medication to which they are not well matched can result in unnecessary side effects, extra physician visits to treat the side effects and change the therapy, and, possibly, disease worsening in the time that it takes to get one medication entirely out of the body and another one in. This means that patients with diseases such as multiple sclerosis and rheumatoid arthritis may experience irreversible changes in their nervous system or joints during the time it takes to work through the "steps" of therapy and reach the medication that is best suited to them. During this time, patients may have lost mobility and quality of life that cannot be regained. Being forced to "fail first" on a cancer medication to which patients are not well matched could be deadly.

Why Not "Fail First"

Medication is determined by the insurance provider and not the physician.

Patients are not individually matched with the medication that is best for them.

Some of the insurance companies' first-choice medications are not as safe for patients as other medications.

Some of the insurance companies' first-choice medications are not approved by the FDA for the condition they are used to treat, which raises safety concerns.

Physicians must spend an inordinate amount of time petitioning the insurance company to allow patients to be treated with medications to which they are best suited.

When the insurance companies' first-choice medications do not successfully treat a patient's condition, the insurance company pays more in the long run.

Patients may undergo unnecessary side effects, hospitalization, suffering, and disease worsening.

Viable Alternative to "Fail First" Policies

Allow physicians to prescribe the medication that is best matched to the patient



Considering biologics and the serious, chronic diseases they are often used to treat, it is truly a case of pay now for the higher-cost medication or pay more later for the lost work productivity, additional medical costs, and disability. Unfortunately, in the pay later scenario, it is our patients who inevitably pay the highest price in terms of lost quality of life, hospitalizations, potentially irreversible symptoms, and disease progression.

The Price Of Patient Safety

Another problem with the fail first policy as it relates to biologics is the sensitivity of these medications to their manufacturing processes. Small differences in the way biologics are manufactured or processed can affect their safety profiles. An example of this is with biologics used for the treatment of certain immune deficiency diseases, in which the immune system cannot adequately fight off infection. Many insurers require that patients fail first on a biologic medication that is associated with an increased risk of blood clots. This is unacceptable because blood clots can lead to hospitalization or even death. In order to help our patients avoid this situation, we must spend time filling out paperwork and contacting insurance companies—time that could be better spent treating our patients. If physicians were allowed to select the medication best matched to each patient, the risk of blood clots could be minimized, not only saving our patients from anguish and suffering, but also avoiding costs associated with hospitalization.

Safety concerns are also raised when insurance policies require that patients fail first on a medication that is not approved by the United States Food and Drug Administration (FDA) for their condition. In some cases, patients must fail first on a non-approved medication before they can get an approved medication. Approval by the FDA indicates that the medication's safety is acceptable when weighed against its potential benefits for a given health condition. Requiring patients to undergo treatment with an unapproved medication to save the insurance company money suggests that the initial purchase price of a medication is valued over patient safety. This puts physicians in the uncomfortable and often unacceptable position of prescribing an unapproved medication without adequate safety documentation over an approved medication with adequate safety documentation.

Ultimately, it is physicians and not insurance companies who have the training, experience, and knowledge of our patients to best determine which medications should be prescribed and in which order. This model, known as segmented or individualized therapy, is an alternative to the fail first model that is often favored by insurers.

Fail first policies are not in the best interest of our patients, nor are they in the interest of overall cost minimization.

Therapeutic Substitution

Therapeutic substitution is another critical consideration with biologics. Therapeutic substitution refers to switching the patient to a different medication than was prescribed by the doctor. This is often initiated by the pharmacist at the direction of the insurance company or a large, chain pharmacy.

Therapeutic substitution is different than generic substitution. When the insurance company or pharmacist attempts to force the doctor and patient to accept a therapeutic substitution, they are actually changing the patient to a different medication than was prescribed. While the switch is often to a drug in the same class, the substitution is done to save the insurance company money or increase the profit for the pharmacy.

As physicians, we prescribe what we believe to be the best treatment for each of our patients, taking into account medical history, other medical conditions and medications, and potential sensitivity to side effects. We know our patients, and have the training and education needed to match the patient to the therapy. In contrast, when pharmacists or insurance companies substitute a different medication, they do so without having the extensive background on individual patients that we employ in our decision making.

With biologics, therapeutic substitution is even more problematic because of the unique aspects of these medications. Many of our most popular and useful biologics are proteins, which have complex 3-dimensional structures that are critically important for their effectiveness.³

The cells or living organisms that make these proteins may differ from one manufacturer to the next and this can impart different biochemical properties to the proteins. Additionally, the protein manufacturing process can affect a product's immunogenicity, or its tendency to stimulate an immune response in patients. Due to their large size and biochemical complexity, biologics are often difficult to characterize with the existing analytical methods.⁴ In these ways, biologics differ profoundly from conventional, small-molecule drugs, which can be thoroughly characterized and compared. For all of these reasons, biologics are not interchangeable with one another and substituting between them is a much more complex undertaking than for conventional drugs and raises serious safety concerns.

“One of my patients with multiple sclerosis had been taking a medication that was inadequate, leaving her open to three exacerbations in one year. We agreed that she should switch to a particular biologic in order to obtain better disease control, but her insurance company required her to first try a different biologic medication. I had not prescribed the medication the insurance company recommended because it has been associated with depression and my patient is already depressed. After four months of appeals, the insurance company finally agreed to authorize the treatment, but the co-pay is 30%, which is prohibitive for my patient.”

Laura Banks, MD
Neurologist



Specialty Drug Tiers

Another important concern with biologic medications is their inclusion on the specialty drug tier of most healthcare benefit plans. Plans typically incorporate several tiers that determine the level of patient cost sharing or the amount of medication cost that must be paid by beneficiaries (i.e., co-pay). The lowest level of cost sharing, tier one, usually includes generic drugs. Tier two, the next higher co-pay level, typically includes preferred name-brand drugs, and tier three includes non-preferred, name-brand drugs. Tier four or the “specialty tier” includes the more expensive drugs such as biologics.⁵

Historically, the amount of cost sharing to be borne by patients has been expressed in terms of a fixed dollar amount. However, plans are increasingly requiring patients to pay a percentage of drug cost for specialty tier medications, which often ranges from 25% to 35%.⁵ In some plans, the co-pay for specialty tier drugs has risen to more than 40%. Given that specialty tier medications can cost between \$10,000 to \$200,000 per patient per year,⁶ this level of co-pay puts these treatments out of reach for many patients.

Typical Medication Tiers In Healthcare Benefit Plans

Tier 1	Generic Drugs
Tier 2	Preferred Name Brand Drugs
Tier 3	Non-Preferred Name Brand Drugs
Specialty Tier	Higher Cost Medications, Including Biologics And Other Injectable Therapies

The specialty tier is viewed by insurers as a money-saving strategy. However, as discussed with the fail-first policy, inadequate treatment of the chronic conditions typically targeted by biologics is itself costly. Studies have shown that biologics can reduce hospitalization,⁷ disease relapses,⁸ and even death.⁹ In some cases, biologics can increase employment¹⁰ or promote a return to normal physical functioning.¹¹ These beneficial effects help to offset the initial purchase price of biologics and may even lead to long-term cost savings for insurers and employers.

Biologics Price Competition and Innovation Act

In an attempt to reduce the costs of biologics, the United States Congress passed the Biologics Price Competition and Innovation Act in 2010. This law allows the approval and marketing of biologics that are similar to the innovators—so-called biosimilars or follow-on biologics. However, the cost savings with biosimilars is not expected to revolutionize healthcare spending. The manufacturing investments and complexity of these medications will still be present, and it is estimated that biosimilars are likely to cost 60% to 80% of the innovator products.^{13, 14} Consequently, many patients will still be unable to afford these medications at co-pay rates of 25-30% and, thus, the specialty tiers and high co-pay rates dictated by insurers will continue be issues with biosimilars.



As physicians, it is frustrating to know that many of our patients cannot afford the biologics that would truly improve their lives. In order to address this problem, we must work to limit the rapidly increasing co-pays for medications on specialty tiers, or even abolish specialty tiers altogether. If insurers were to take into consideration all of the costs of chronic diseases, the value of biologics could be better estimated. Conversely, the costs of ineffective treatment must also be considered. When these are added to the purchase price of conventional drugs that offer only minor symptomatic improvements to patients, the true costs of these “inexpensive” products are unacceptably high.

Different Therapies Require Different Benefit Designs

Levels At Which Biological Products Show Greater Complexity Than Conventional Drugs

Size and structure

Biochemistry

Manufacture and production

Characterization and analysis

Shipping and handling

Dosage and administration

Immunogenicity

Side effects and safety

Characterization and analysis

Biologics can provide meaningful benefits for patients that often cannot be obtained with other types of therapies. However, these benefits come with greater complexity at multiple levels, as shown in the following table.

Given the differences between biologics and conventional drugs, it is not surprising that the US Congress has seen the need to pass special legislation pertaining to biosimilars; the government and the United States Food and Drug Administration recognize that biologics cannot be treated the same way as conventional drugs.

We now need to address critical aspects of healthcare benefit plans that interfere with or even block patient access to biologics. “Fail first,” therapeutic substitution, and specialty tier policies do not exist for the purpose of providing patients with the best care. These policies exist simply to cut costs or increase profits for insurance companies or pharmacies. Nor are these policies economically rational if one considers patients and their diseases in their entirety. With the healthcare changes underway in our nation, we have the opportunity to develop new policies for this unique class of therapies.

Patients must be able to access the biologics prescribed by their physicians that can meaningfully treat their diseases and better their lives.

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