The US Biosimilars Perspectives
Gottlieb Calls On Congress To Act On US Biosimilars Uptake

Executive Summary
Calls to give up on biosimilars in the US are premature, former FDA commissioner Scott Gottlieb insists. Rather, he says, Congress should act to promote uptake and greater competition in the biologics arena.

The US Congress can make “straightforward changes to speed the development and use of cost-saving biosimilars,” former US Food and Drug Administration commissioner Scott Gottlieb has argued in an opinion piece published in the Wall Street Journal. Gottlieb was responding to an earlier article by Peter Bach and Mark Trusheim that suggested it was “time to throw in the towel on biosimilars.”

Outlining his proposals for legislative fixes, Gottlieb says Congress could first “pass a law mandating that brand companies sell their biologic drugs at a fair market price to biosimilar manufacturers seeking to develop copies.” Draft legislation to this effect, in the form of the bipartisan Creating and Restoring Equal Access To Equivalent Samples (CREATES) Act, is currently before Congress.

“A biosimilar manufacturer typically needs hundreds, and sometimes thousands, of doses of the originator product to run the required FDA trials to prove that their copycat drug can be used interchangeably with the original biological medicine,” Gottlieb observes. “Some brand drugmakers block such sales. They have an incentive to make it harder for biosimilar manufacturers to clear basic regulatory hurdles.”

Ways To Protect Against Unsafe Use Of Samples
Addressing arguments that samples sold to biosimilar developers might get resold in unsafe ways, Gottlieb argues that the FDA can ensure drugs are not used in unintended ways, while Congress could indemnify originators against any risk arising from use of their samples in biosimilarity trials.

Second, Gottlieb proposes, “Congress can stop branded drug companies from using ‘rebates’ to squelch competition from biosimilars.” Describing such kickbacks as “a big inducement” for insurers to prefer original biologics, the former FDA commissioner notes that “if a health plan were to adopt a biosimilar, it might void its rebate contracts for biologic drugs and lose payments.”

“Rebates take years to get in place and a new entrant may be hard pressed to offer insurers a similar deal,” he recognizes, pointing out that such inducements can be anti-competitive if used to block access to lower-cost generics and biosimilars.

Reforms proposed by the Trump administration would have removed a ‘safe harbor’ provision that currently exempts rebates to pharmacy benefit managers and the federal Medicare Part D program from the Social Security Act’s anti-kickback statutes. However, the proposals were shelved over fears that could increase Medicare drug-insurance premiums.

“Drugmakers developing biosimilars, including one branded company I advise, are arguing safe harbor should be eliminated,” recounts Gottlieb, who now describes himself as “an investor in, and director of, drugmakers.”
**Educational Investment Sorely Needed**
Third, Gottlieb believes the US must invest more heavily in educating doctors about the safety and effectiveness of biosimilars and the value that they can deliver to patients and the healthcare system. He recalls how prescribers’ initial unfounded fears over the reliability of small-molecule generics were overcome to the extent that generics now account for around nine out of every 10 prescriptions filled. “The same initial trepidation is slowing adoption of biosimilars and costing patients billions,” he asserts.

“The opportunity offered by biosimilars is still unfolding,” Gottlieb concludes. “But the value they can offer is clear. Congress should take new steps to accelerate their adoption.”

Responding to Gottlieb’s opinion piece via Twitter, Bach – director of the drug pricing lab at Memorial Sloan Kettering Cancer Center – argued that issues around biosimilars uptake should not be conflated with those for small-molecule generics.

“The regulatory problems for small-molecule generic entry can be solved. Congress has a hard time doing so, but the glide path is clear,” Bach insisted. “The problem with biologics has to do with the difficulty and cost of replicating them, and the regulatory fog is thicker as a result.”

**Originators ‘Shape-Shift’ On Defensive Strategies**
Bach also suggested that the complexity of the US pricing, reimbursement and regulatory landscape around biologics enabled originators to “shape-shift” in their defensive strategies, thereby raising the cost of biosimilar market entry and “ruining competitive possibility.”

In his WSJ opinion piece with Trusheim, Bach had reiterated many of the arguments he had made earlier in Health Affairs blog posts in which he proposed abandoning attempts to create a viable US biosimilars market in favor of regulating original biologics’ prices post-exclusivity.

Predicting that the FDA’s “onerous testing requirements” for biosimilars might result in “only two or three competitors” for reference biologics, Bach and Trusheim claimed this would “exert only mild price pressure on the original drug.” They cited Biosimilars Council forecasts of $50bn savings from biosimilar competition over the next decade, “about what we believe could be saved each year through price regulation.”

Furthermore, they argued, clinical studies for biosimilars “slow the pace of innovation” by diverting participants away from studies into novel therapies.
Do Not Throw In Towel On Biosimilars, Says New Sandoz Chief

Executive Summary
Assertions that the US should give up on supporting biosimilars in favor of controlling prices of off-patent biologic brands fail to recognize promising signs of progress, argues Richard Saynor, who has just taken over as CEO of biosimilars pioneer Sandoz.

US policymakers and healthcare stakeholders must not give up on biosimilars, but rather build on some promising recent developments and trends that could unlock vast savings, insists Richard Saynor, who has just taken up the post of CEO of biosimilars pioneer Sandoz.

Reacting to a Wall Street Journal article in which oncologist Peter Bach and colleague Mark Trusheim argue that biosimilar competition would harm innovation without creating meaningful healthcare savings, Saynor points out that the same doubts about the ability of competition to drive savings were voiced loudly when the US generics market was effectively created by the Hatch-Waxman Act in 1984. At the time, some proponents argued that the competition would not work in the complex pharmaceutical sector, so price regulations were needed.

“Today, as biosimilars look increasingly like the ‘new generics’, it’s fascinating to watch the same tactics being deployed against them,” he remarks, pointing out that generics now make up 90% of all US prescriptions filled but account for just 22% of medicines spending, thereby saving $2 trillion over the past decade.

Same Tactics Were Deployed Against Small-Molecule Generics
Acknowledging that former US Food and Drug Administration Scott Gottlieb has rebutted Bach and Trusheim’s arguments and put the onus on the US Congress to address barriers to biosimilar usage, Saynor notes that the timing of the debate coincides with several positive developments.

“Perhaps the most interesting thing about this argument is its timing: it comes just as the biosimilars market is actually gaining traction in the US, and after a decade of strong performance in the European Union,” he observes. “Indeed, we are seeing consistently greater uptake with each new biosimilar launch in both Europe and the US, as shown by leading financial analysts.”

As an example of how US payers and insurers were reacting rapidly to opportunities to realize savings through competition, Saynor references a recent announcement by United Healthcare, which covers 50m Americans, that it would prefer Amgen’s Kanjinti (trastuzumab) biosimilar over Roche’s Herceptin reference brand for commercial and community plans. Amgen’s Mvasi (bevacizumab) biosimilar is also to be preferred to Roche’s Avastin. (Also see “US Insurer United Rewards Amgen’s Early Entry With Bevacizumab And Trastuzumab” - Generics Bulletin, 21 Aug, 2019.)

Market-Leading Zarxio Filgrastim Preferred
Also from 1 October, the insurer will for the same group of members prefer Sandoz’ Zarxio (filgrastim-sndz) to its rival biosimilar, Pfizer’s Nivestym (filgrastim-aafi), as well as to Teva’s Granix (tbo-filgrastim) follow-on version of the
neutropenia treatment and to Amgen’s Neupogen reference brand. Saynor described this move as “bolstering a category where the market leader has become a biosimilar, and where two-year savings for that one medicine are over half a billion dollars.”

Observing the major role debates over drug pricing are playing in the upcoming US elections, Saynor highlights the key role biosimilars are playing in making the US system more sustainable. “Policies continue to encourage biosimilar development, such as the recent Centers for Medicare and Medicaid Services guidance enabling biosimilars to receive their own healthcare common procedure coding system (HCPCS) reimbursement code,” he states.

But while momentum is building behind biosimilars in the US, he recognizes the many challenges to be overcome, in areas such as reimbursement and misinformation. In this latter area, he identifies a bias in Bach and Trusheim’s ‘throw in the towel’ WSJ article.

“The authors state that biosimilars can’t be identical to reference medicine biologics, citing the complexity of production. In reality, though, it’s a well-understood scientific fact that even reference medicine biologics aren’t identical to themselves batch to batch,” he objects.

“Finally,” Saynor concludes, “it’s worth spelling out what that proposal in the WSJ opinion piece is really saying. Effectively, the message is that the US should ‘give up’ on competition and rely on the government to regulate the market. As a British citizen who knows and loves the US, that doesn’t sound like the America I know!”

Bach and Trusheim’s opinions have elicited critical responses not just from the biosimilars industry and Gottlieb, but also from the originator side.

**Giving Up Would Be Bad For Patients**

In a letter sent to the WSJ, Stephen Ubl, president and CEO of US originators’ body PhRMA, condemns giving up on biosimilars as “shortsighted and bad for patients and provider choice.”

“Already, biosimilars have been yielding significant benefits, restraining costs and improving patient affordability. While biosimilars are in their infancy, these benefits will grow over time as more are introduced,” Ubl argues.

“Every specific biologic referenced by the authors already is subject to competition from biosimilars that have much lower prices than the innovator products,” he points out. “One example omitted in the cases cited are biosimilars used to treat neutropenia, which now account for 63% of the market, and their price has dropped 38% since launch.”

In a separate letter, pharmacist Rita Shane from Los Angeles’ Cedars-Sinai Medical Center highlights the practical implications for hospitals and clinics of various insurers preferring different versions of biologic molecules, based on what level of rebates they had secured from the manufacturer.

“As of June,” she observes, “trastuzumab, used for breast cancer, has five biosimilars, and pegfilgrastim, used to prevent life-threatening infections in cancer patients, has two biosimilars.”

**Insurer Rebates Increase Complexity For Clinics**

“By using rebates, each of the eight companies which make these two drugs can secure insurer-preferred status, creating a new paradigm for
treatment,” she points out. “Besides prescribing the most effective chemotherapy regimen, physicians will need to verify that the drugs are correct based on the patient’s insurance.” She argues that the greater number of vials needed to be held in stock by cancer clinics would increase “the risk of mix-ups since biosimilars look alike.”

With clinicians needing to ensure insurance-specific drugs are prepared, dispensed and administered correctly, essential treatment could be delayed if the required biologic brand is not in stock, she warns.

“Rebate-driven insurance requirements by drug manufacturers not only increase health-care costs; they also increase the risk of harm to vulnerable patients,” Shane concludes.
US Employers Could Cut Costs By Encouraging Biosimilar Usage

Executive Summary
Promoting the use of biosimilars among their employees to whom they provide health insurance could reduce their costs for specialty drugs by more than a tenth, an analysis of real-world claims data suggests.

US employers could cut more than a tenth off their specialty drug spending via medical benefits for employees by supporting greater usage of biosimilars, according to a case study of a large manufacturing company conducted by Matrix Global Advisors and the National Business Group on Health.

The case study, which is sponsored by Boehringer Ingelheim, uses real-world claims data from an undisclosed manufacturing company with a high-deductible medical benefits plan covering more than 80,000 members. An analysis shows that, in 2017, 392 plan members used at least one of 17 biologic drugs that already face, or will soon face, biosimilar competition. Employer spending on these biologics was more than $9.3m, in addition to out-of-pocket costs for patients exceeding $500,000, with Avastin (bevacizumab), Herceptin (trastuzumab) and Neulasta (pegfilgrastim) all costing the employer more than $1m in 2017, while spending on Remicade (infliximab) was over $3m.

Recognizing potential variances in price discounts and utilization rates, the researchers model three scenarios:

- Base case: Assumes 30% biosimilar substitution rate at a 30% price discount to the reference biologic.
- Optimistic case: Assumes 50% biosimilar substitution rate at a 40% price discount to the reference biologic.
- Best case: Assumes 75% biosimilar substitution rate at a 40% price discount to the reference biologic.

Estimates of total annual savings for the employer range from $0.838m to $2.793m, equating to an average saving of $2,137 to $7,125 across the 392 patients taking biologic drugs. Across the more than 82,000 plan members, the annual employer’s savings per plan member run from $10 in the base case to $34 in the best-case scenario.

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“Employer savings in the three scenarios represent 3.2%, 7.1% and 10.7% respectively of the employer’s specialty drug spending in the medical benefit,” the case study states. In addition, patients taking biologic drugs stand to save $121 to $403 per year in out-of-pocket costs.

“By itself,” the authors Alex Brill and Christy Robinson acknowledge, “an employer has limited opportunities to shift behaviour. But an employer could share a portion of their own savings from biosimilar use with members,” they suggest. Proposing that an employer could urge its health plan to encourage biosimilar usage through plan design, as well as incentives and education for both physicians and plan members, they claim that their savings estimates “can serve as a guide for how much an employer may want to invest in promoting biosimilar utilization.”

**Several Factors Are Limiting Uptake**
Highlighting the importance of employers in promoting biosimilar uptake, Brill and Robinson suggest several factors have contributed to a “sluggish launch” of the biosimilars sector in the US. These factors include “market uncertainty, the threat of patent litigation, development cost, reference product manufacturers’ efforts to retain market share, and a lack of physician and patient education about biosimilar safety and savings.” In particular, they point to a lack of incentives within the federal Medicare system for physicians to favor lower-cost drugs.

Reacting to the analysis sponsored by its member company Boehringer Ingelheim, the Biosimilars Forum identified employers as among an array of market participants that could help to create a competitive and sustainable biosimilars market in the US.

“Multi-stakeholder engagement – from Congress and the White House to physicians and payers – is crucial to overcoming barriers that inhibit the US biosimilars market from taking hold,” insisted the Biosimilars Forum’s president, Juliana Reed. “Given their unique positioning to negotiate health-plan designs with providers, employers are integral to this effort.”

Without such stakeholder engagement, Reed warned that considerable savings potential would go untapped. “As originator biologics continue to monopolize the market, we are at risk of a future where there is no competition from biosimilars in the US market.”

**Throwing In The Towel Would Be Harmful**
Given the current public and political concerns around drug costs, the Forum argued that suggestions of ‘throwing in the towel’ on biosimilars made in a Wall Street Journal article would be harmful and would cost US seniors and taxpayers up to $71bn in missed savings.

In their WSJ opinion piece, Memorial Sloan Kettering Cancer Center colleagues Peter Bach and Mark Trusheim argued that the US biosimilars market was failing deliver meaningful savings, so regulating the prices of off-patent biologic brands would be more effective. (Also see “Gottlieb Calls On Congress To Act On US Biosimilars Uptake” - Generics Bulletin, 27 Aug, 2019.)

This drew a response from former Food and Drug Administration commissioner Scott Gottlieb, who called on Congress to remove barriers to biosimilar competition. New Sandoz CEO Richard Saynor also accused Bach and Trusheim of failing to recognize signs of significant progress being made in promoting the use of biosimilars in the US. (Also see “Do Not Throw In Towel On Biosimilars, Says New Sandoz Chief” - Generics Bulletin, 29 Aug, 2019.)
“Current policies are distorted to disincentivize lower-cost biosimilars,” the Biosimilars Forum asserted in response. “While changing them is a common-sense solution to deliver savings, instituting price controls for biologics already on the market is not.”

Citing savings running to billions of dollars in Europe, the Forum stressed that “we know from experience the claim that biosimilar competition won’t lower costs is flatly untrue.”
US Distributor Demands Better Biosimilars Support

Executive Summary
Removing legal hurdles and putting biosimilars on preferred formulary tiers will increase access and cut the cost of biologic therapies in the US, argues the chief of major healthcare distributor AmerisourceBergen.

A more supportive system is needed to drive greater uptake of biosimilars and generate healthcare savings in the US, according to a letter sent to the Wall Street Journal by AmerisourceBergen’s chairman, president and CEO Steve Collis. The letter from the chief of the US distributor is the latest in a string of responses to an opinion piece in which oncologist Peter Bach and colleague Mark Trusheim suggested it was time to “throw in the towel” on biosimilars in the US and focus on controlling prices of off-patent biologic originals.

“If we remove legal hurdles, push for preferred formulary status and establish a clearer path to interchangeability, we can facilitate uptake, thus creating access and affordability,” Collis argues in his letter.

Highlighting experiences with biosimilar uptake in Europe, Collis points out the impact competition has had on “driving down prices of entire therapy classes.” “The European Union experienced success once it enabled biosimilars to reach patients,” he highlights. (Also see “US Must Learn Lessons From Europe On Biosimilars” - Generics Bulletin, 25 Mar, 2019.)

Conditions Exist For Commercial Success
Recognizing the “marked differences” between US and EU economic and healthcare systems, Collis nevertheless insists that “the right conditions exist in the US for biosimilar commercialization success.” He points out how competition in the small-molecule generics sector has pushed down prices over the past 30 years.

But as in the generics sector, he believes Congress must act to provide impetus to biosimilars uptake. Former Food and Drug Administration commissioner Scott Gottlieb has also, via the WSJ, called on Congress to remove barriers to greater biosimilar usage.

Collis observes that “the Prescription Drug Pricing Reduction Act slated for Senate review this fall creates incentives to use biosimilars, with the most notable provision allowing biosimilars to receive a higher reimbursement rate than reference products.”

Section 104 of the proposed PDPRA legislation, which was scheduled for mark-up by the Senate’s finance committee in late July this year, would establish a payment rate for biosimilars furnished on or after 1 July 2020 for around six months that would be the lesser of the biosimilar’s wholesale acquisition cost plus 3% or the biosimilar’s average sales price plus 6% of the reference biologic’s ASP.

Bipartisan Bill Would Raise Biosimilar Payments
And Section 105 would raise the add-on payment for a biosimilar under Medicare Part B from the
current 6% of the reference biologic’s ASP to 8% of the original’s ASP for a period of five years.

At that time, a Congressional Budget Office assessment calculated savings from Section 104 at only $1m per year, but was unable to put a figure on the impact of Section 105.

The bipartisan bill also requires prescription drug, biological, and biosimilar manufacturers that do not have a Medicaid drug rebate agreement to report average sales price information to the Secretary of Health and Human Services that would be used to help establish Medicare payment rates.

Even without Congressional action, Collis welcomes the steps being taken by private payers to adopt biosimilars, such as the recent move by UnitedHealthcare to award preferred formulary status to Amgen’s Kanjinti (trastuzumab-anns) and Mvasi (bevacizumab-awwb) biosimilars following their ‘at-risk’ market entry amid ongoing patent litigation. (Also see “US Insurer United Rewards Amgen’s Early Entry With Bevacizumab And Trastuzumab” - Generics Bulletin, 21 Aug, 2019.)

“Legislators and commercial plans are clearly seeing the potential value. Manufacturers continue to invest because the system is starting to work,” Collis concludes. These sentiments are similar to those expressed by Sandoz’ new chief, Richard Saynor, in response to the WSJ debate. (Also see “Do Not Throw In Towel On Biosimilars, Says New Sandoz Chief” - Generics Bulletin, 29 Aug, 2019.)

In a separate letter to the WSJ, the executive director of non-profit advocacy group Patients Rising, Terry Wilcox, responds to Bach and Trusheim’s arguments, as well as to Gottlieb’s response, by insisting that “eliminating rebates, which have turned the prescription-drug supply chain into a pay-to-play system, is a better way to create a robust supply of cheap biosimilar therapies than introducing price controls on older biologics.”

“Biosimilar manufacturers that cannot afford to pay the hefty rebate pay-outs to pharmacy benefit managers cannot access drug formularies, even if their products are cheaper,” she highlights. As FDA commissioner, she notes, Gottlieb had identified this factor as a key reason why biosimilars were struggling for market access, thereby leaving annual savings of more than $4.5bn on the table.

“If potential biosimilar manufacturers can’t get their product to market, they won’t proceed with development,” points out the director of Patients Rising, which is supported by both original biologics and biosimilars players such as Amgen, Celgene, Janssen, Novartis and Pfizer.

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