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WHITE PAPER

Biosimilars and Interchangeability:

Has the time arrived?

In case you missed it, the FDA approved Semglee® (insulin glargine-yfgn; Mylan) on July 29,2021 as the first interchangeable biosimilar product in the US market. While interchangeability is new for Semglee, the product is not, having been approved via the 505(b)(2) pathway in June, 2020. So if the product itself isn't new to the market, the question becomes what value does "interchangeability" confer and should we be relying on the insulin class as the proving ground for interchangeable specialty biosimilars?

To address the question of interchangeability and generic substitution, it's natural to jump to oral, small molecule products which are self-administered. This market behaves rationally as branded products facing multi-source generic competition are rapidly commoditized leading to broad payer adoption of generic substitution. This formulary design is borne out through pharmacy software and operating systems which broadly accept interchangeability and in fact drive the substitution process. Which brings us to the key question of biosimilar interchangeability: should we make the assumption that the biologics market will behave rationally?

To understand the unique dynamics of the biologics/ biosimilars space, we need to break out the marketplace dynamics which are key influences into the likely behavior and adoption of the market to interchangeability:

- **First is the question of formulation:** Insulin glargine is currently a three-player market with Lantus® (Sanofi, approved 2000), Basaglar® (Lilly, approved 2015), and Semglee (Mylan, approved 2020) currently available in the market. Basaglar and Semglee were both approved via the 5050(b)(2) pathway with Semglee receiving interchangeability approval for Lantus as a reference product on July 29th. Lantus and Semglee are available in both vial and prefilled pen presentation while Basaglar is only available as a prefilled pen. Vial is an important differentiator within specific care settings (e.g. hospital inpatient) due to the high incidence of needlestick injuries with caregivers.
- **Second question is regulatory:** States regulate the ability of pharmacists to substitute interchangeable products during dispensing activities. Within the current regulatory environment, we have a patchwork of regulations both allowing and prohibiting pharmacist substitution by interchange. States have historically relied on the FDA Orange Book for small molecules which include clear indicators of therapeutic equivalence and readily aligns to pharmacy operating systems. The FDA Purple Book for biologic products is less intuitive, leading to third party payers to drive product substitution or pharmacists to keep current with all interchangeability allowances for biologic products. We're good, but we're not that good…
- **Third question is affordability:** Biological products are expensive. They're commonly third-tier or higher within plan formularies and are the workhorses of the specialty tier. This translates to higher patient out-of-pocket cost and the need for manufacturers to carefully consider what patient access and support services (PASS) are required. We're seeing specialty generics and biosimilars launch commercial copay support programs with new launches, but if we're empirically expecting biosimilars to start at a lower price point, the impacts of launching a commercial copay program can make gross-to-net management a challenge.
- **Fourth and most importantly coverage**: Insulin coverage is heavily influenced by retrospective third-party payer rebates. Within the insulin glargine class specifically, analysts estimate that rebates are >80% of manufacturer

list price. This is where the rationality argument comes in: does coming to market with a lower list price drive utilization when rebates make the net economics of the innovator cheaper net-net? If past experience forecasts our future expectation, I think we can make some inferences here.

- **The final and likely most important aspect to the whole discussion:** we're talking about insulin. At the end of the day, there may not be a more directly linked molecule to a real-time efficacy measurement. You can track your blood glucose on a smartphone in real time and can send results to your physician via electronic health record portal. There's no mystery to whether the product is working based on a bona fide home-based measurement which doesn't exist within other specialty biologic treatments.

If we can't assume that insulin glargine will behave rationally, then applying the same logic to specialty biologics is futile. We applaud Mylan for pursuing the pathway and the FDA for establishing a framework to have these discussions in the first place, but specialty will introduce even more pronounced challenges to those faced by Semglee. In this market, interchangeability becomes exacerbated by patient and provider formulation preferences, injection device preferences, state-level regulatory limitations, third-party rebate structures, and decisions whether to "grandfather" established vs. stable patients. Destabilization of existing patients on therapy may introduce new medical spend which exceeds the pharmacy cost savings in the first place.

There's a range of critical considerations when commercializing products within this space, and while our industry is still in the early stages of navigating this change need to be realistic about limitations of interchangeability. These limitations raise the requirement of generic manufacturers to more deeply understand the market to navigate successful biosimilar or specialty generic launches have increased. Teams need to take a branded product management philosophy and double click on the impact of channel, Patient Access and Support Services (PASS) and dispensing economics as drivers for product selection and utilization. Branded manufacturers must build generic competitive launch planning into brand lifecycle management for both biologic and small molecule products where the influence of generic channel and PASS offerings can have profound impacts. As a collective industry, we need to more fully understand the policy and financial impacts of strategic decisions on providers, dispensers and patients.

We have a great privilege to live and work in an incredibly interesting and complex marketplace. The work we do today to further understand the healthcare ecosystem lays the groundwork for charting our future.

The Author

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Andy holds a Bachelor of Science from the University of Wisconsin, Stevens Point and a Doctor of Pharmacy from the University of Wisconsin, Madison. He has served on national committees focused on pharmacy operations and quality initiatives and has been actively engaged with dispensers and care providers in optimizing internal dispensing models.