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Economics Of Harm From Biologic-Biosimilar Competition

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For more than two decades and despite the Biologics Price Competition and Innovation Act of 2009, the Hatch-Waxman brand-generic disputes have dominated the life sciences competitive landscape. However, a new and highly anticipated biologic-biosimilar competition is finally a reality: look no further than the recent launch of Sandoz's filgrastim biosimilar Zarxio and anticipated launch of Celltrion's infliximab biosimilar Inflectra. The advent of this new type of competition is a big deal: in the U.S. alone, biologics market is estimated at more than $140 billion and more than 20 biologics with a market value of over $50 billion will lose patent protection by 2019. More than 50 percent of the U.S. prescription drug budget is expected to be biologics by 2018 and it is estimated that 40 percent of all pharmaceutical industry R&D and products in the pipeline involve biopharmaceuticals rather than traditional drugs.[1]

The economic insights and tools related to pharmaceutical competition developed during the decades of brand-generic Hatch-Waxman disputes will be useful in analyzing biologic-biosimilar competition in BPCIA disputes. However, insights and tools developed and routinely applied by economists in the contexts of small molecule brand-brand (e.g., Lipitor-Zocor) and brand-branded generic (Wellbutrin XL-Budeprion XL) competition and biologic brand-brand (e.g., Humira-Enbrel) competition will be also valuable in BPCIA disputes.

For example, with the goal of obtaining a permanent injunction, Janssen Biotech Inc. recently requested that the court schedule trial in its litigation relating to the biologic infliximab, prior to the anticipated at-risk launch of Celltrion's U.S. Food and Drug Administration-approved biosimilar Inflectra in October 2016.[2] As part of injunction or restraining order submissions, economists often assist courts with the question of irreparable harm. For a number of reasons, an economic analysis of irreparable harm for biologic-biosimilar competition, such as between Remicade and Inflectra, will use insights and tools developed by economists in the contexts of small molecule brand-brand and brand-branded generic competition and biologic brand-brand competition rather than from the small molecule brand-generic competition alone.

An examination of the market reaction to the co-availability of Amgen's Neupogen and the first U.S. biosimilar, Sandoz's Zarxio, suggests that it is likely that the harm to Janssen Biotech from the potential launch of Inflectra, while significant, may not be the same in scope and pace as that typically expected in the small molecule brand-generic competition context. An analysis of Zarxio following its launch shows that after its first four months, the biosimilar has taken only 24 percent of Neupogen's prescription

volume, compared to a more typical 75 percent penetration of a brand's volume four months after a small molecule generic entry.[3] In other words, based on the Neupogen-Zarxio case study, it appears that competition in the biologics market more closely resembles brand-brand competition rather than brand-generic competition in the small molecule drug market.[4]

For an economist, such a result is not surprising and should have not been unexpected. One of the critical mechanisms through which a small molecule brand loses its sales and profits after generic entry is automatic generic substitution at a pharmacy level. For biosimilars, automatic substitution does not occur unless the biosimilar shows "interchangeability" with the reference product. Interchangeability requires additional studies and testing to establish that biosimilar and the reference product are expected to produce the same result in the same patient and can be switched out for each other without any impact on safety or effectiveness. Because of the additional effort required to show "interchangeability," it is not expected to be typically part of biologic-biosimilar dynamic immediately after biosimilar launch. Even in the case of Sandoz's Zarxio, a relatively simple protein compared to Celltrion's Inflectra, Sandoz did not apply for direct interchangeability.[5] Because biosimilar manufacturers will likely forego, or at least delay, applying for interchangeability, biosimilars will not enjoy the automatic substitution that helps drive sales of generic products in the small molecule drug market.[6]

Another mechanism through which a small molecule brand loses its sales and profits after generic entry relates to the preferential formulary status, reimbursement and copay incentives available for generics. It is predicted that in most cases such incentives will not be available for biosimilars. For example, because biosimilar products do not meet the definitions of "generic" or "multiple source" drugs under either the Medicare or Medicaid programs, the Centers for Medicare and Medicaid Services has determined that biosimilars will be treated as "single source" drugs and are subjected to separate coding, higher copayments for beneficiaries and higher Medicaid rebate obligations for manufacturers than if they had been characterized as noninnovator products.[7]

Additionally, regulatory differences related to biosimilars and generics naming conventions and labeling regulations versus their reference products may inhibit rather than encourage a biosimilar's capture of brand sales.[8] For example, under current FDA guidance, a biosimilar product will be referred to by the name of the biologic plus a differentiating suffix, e.g., "filgrastim-sndz," which could cause confusion among prescribers and patients.[9]

Biosimilar product launches, such as the anticipated launch of Inflectra later this year, are expected to pick up pace. As the launch of biosimilars in the U.S. picks up momentum, so too will the number of high-stakes biologic-biosimilar disputes. The traditional economic analysis employed for Hatch-Waxman brand-generic disputes, while still useful, will not be sufficient to guide irreparable harm and other economic analysis in this new life sciences competitive landscape. It is critical that sound economic tools and insights from cases across life sciences are used in biologic-biosimilar disputes.

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[1] http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732 (viewed 4/18/16) and https://www.ftc.gov/system/files/documents/public_events/Follow-On%20Biologics%20Workshop%3A%20Impact%20of%20Recent%20Legislative%20and%20Regulatory%20Naming%20Proposals%20on%20Competition/purvis.pdf (viewed 4/18/16).

[2] Docket Entry 140, Janssen Biotech Inc. et al. v. Celltrion, Inc. et al., No. 15-cv-10698 (D. Mass). The U.S. marketing of Inflectra will be handled by Pfizer. http://www.law360.com/articles/783858 (viewed 4/14/16).

[3] http://www.law360.com/articles/783512 (viewed 4/14/16).

[4] Similarly, contrary to a typical generic product development experience, Celltrion claims to have spent substantially more than $100 million developing its biosimilar to Remicade for which it is seeking or obtained approvals in 70 countries. http://www.law360.com/articles/609573 (viewed 4/14/16). In 2011, a spokesman for Novartis, commenting on the company's own experience with biosimilars, stated that it currently takes, on average, about seven years and approximately $200 million to develop a biosimilar product. http://www.law360.com/articles/227759 (viewed 4/14/16).

[5] http://www.law360.com/articles/628468 (viewed 4/14/16).

[6] The four categories of similarity used by the FDA are not similar, similar, highly similar, and highly similar with fingerprint-like similarity. http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm397017.pdf (viewed 4/14/16). FDA generally takes a negative position regarding a biosimilar applicant's ability to establish interchangeability in an original application. http://www.fda.gov/downloads/Drugs/.../Guidances/UCM273001.pdf (viewed 4/14/16).

[7] http://www.law360.com/articles/784892 (viewed 4/18/16).

[8] See, for example, http://www.law360.com/articles/682940 (viewed 4/14/16) and http://www.law360.com/articles/659971 (viewed 4/14/16). Other common arguments - for example, biosimilar's sponsor's inability to pay likely damages award and biologic's sponsor's salesforce and other employee layoffs and loss of research and development dollars - require a more detailed, case-specific context to analyze.

[9] See, for example, http://www.raps.org/Regulatory-Focus/News/2016/01/21/23947/PhRMA-BIO-Double-Down-on-Biosimilar-Naming-With-FDA-Petition/ (viewed 4/15/16).

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