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Business Development & Licensing Journal

Pricing & Access Trends for Biosimilars a & Innovative Biologics

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Pricing & Access Trends for Biosimilars and Innovative Biologics in Europe

The emergence of biosimilar medicines raises pressing questions for business development & licensing executives

What market potential can we expect of a biosimilar drug, given the pricing and market access landscape of the originator biologic, the therapeutic environment, the competition and the payer regulations? What plans can we make for a launch, perhaps several years in the future, with such a dynamically changing environment? And, perhaps most disruptively, what if my originator compound enters a market where the payer-relevant comparator is a biosimilar?

Chris Shilling & Andras Incze

Akceso Advisors AG

Forecasting the market potential for biosimilars and novel drugs entering markets where biosimilars are already available is a delicate combination of art and science.

To be prepared for your BD&L decision, you have a multitude of information sources available to you. Here we have compiled key relevant aspects from secondary literature research, recent pricing & access due diligence projects we have conducted and a live payer-pharma event that we recently organised.

Akceso Advisors hosted our second Payer & Pharma Networking Meeting event in May 2017 at the Hungarian Embassy in Bern, Switzerland. The event, attended by executives from several large and small pharmaceutical companies, provided an opportunity for payer and industry representatives to consider issues affecting the adoption of biological medicines.

Ambassador Nagy
Payer & Pharma Networking Meeting
May 2017

About the Authors

Andras Incze - CEO of Akceso Advisors, Andras has extensive experience with pharma managing P&R in over 100 countries. He has launched P&R over 15 compounds in corporate role, and advised on countless more. He has designed Patient Access Programs in emerging economies, as well as developing pricing models & tools, and due diligence methodology. Former Head Sales & Marketing Productivity & Head Global Capital Management at Novartis. He is co-author of book on health economics, pharma pricing and market access.

Chris Shilling - has 20 years' experience in Pfizer, Novartis & biotech companies, and as adisor with Akcesco. He is programme committee Chair for the EU Industrial Research Management Association, SME advisor for UK/EU government, NGO and Patient Organisation policy projects. He has led the Pfizer's Global Business Innovation Unit to develop new drug commercialization models.

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Our panelists were:

Dr Tamás Szamosi, Advisor at NEAK Special Fund – the Hungarian National Payer, a leader in biosimilars access management

Prof Jaime Espín-Balbino, EU Principal Investigator – Expert on new methodologies for Health Technology Assessment, Spain

Mr Darius Panaligan MBA, VP, Global Head of Commercial, Merck Biosimilars

Dr András Incze, Akceso's Founder & CEO

Access to Medicines

Dr Szamosi & Prof Espín both highlighted the disparate adoption rates for biological drugs in the EU. Prof Espín's work shows the time to actual market entry following approval in the EU has been between 3 months and 14 years for a biologic, while for a biosimilar it is between 1 and 25 months.[i] Dr Szamosi showed a specific example of the significant difference in access to Chron's disease biologics across CEE countries.[ii]

Payers currently tend to focus on potential savings from aggressively adopting the use of biosimilars, particularly by tendering for them.[iii] Health economic models are emerging to illustrate the cost savings, e.g. the OHE's model of introducing a breast cancer biosimilar[iv] and a recent budget impact model for biosimilars in Italy,[v] although evidence from a study in Belgium suggests that savings vary significantly by country.[vi]

> "slowly flexible rather than inflexible process"

The real question in adopting biosimilars should perhaps be 'how many more people can have access to medicines', with research already suggesting that this value proposition is a strong one.[vii]

Who benefits from savings?

With the patents of several 'Standard of Care' drugs due to expire soon, biosimilars do undoubtedly offer a major opportunity for cost saving. However, each country has a different approach to using those savings.

In the USA, research suggests that payers – health insurers – are most likely to benefit from the savings produced by adopting biosimilars, with only a small percentage of savings passed on to the patient.[viii] There are clear opportunities for savings and better access in Asia,[ix] but complex distribution models in several Asian countries mean it is not clear whether patients benefit from the discounts achieved.

Spain operates a specific hospital drug budget - any savings have to be spent on medicines. A hospital's drug budget manager is responsible for managing the trade-off in meeting larger patient need with biosimilars to be able to treat patients with new drugs that deliver improved outcomes. The new Hepatitis C treatments are funded by savings made using biosimilars.

In Hungary's largely centrally managed system, any savings have to be used in the same field; if money is available in the system then a new drug can benefit from this opportunity. Described as a "slowly flexible rather than inflexible process", system change to enable additional funding for pharmaceuticals only happens by government intervention; using money saved by adopting biosimilars is a good way to fund the introduction of innovative new drugs.

Containing Costs – Biosimilar Managed Entry Agreements?

Payers are concerned about how to manage the threat of increasing volume without a commensurate drop in price when adopting biosimilars. Recent evidence showed an increase of over 250% in the use of biological agents following the introduction of biosimilars.[x]

Managed Entry Agreements (MEAs) are now well accepted as a tool for enabling the staged adoption of innovative drugs, but there is little clear experience of how MEAs might be applied to biologics. A 2011 Hungarian study shows that negotiation on a drug-by-drug basis can produce positive outcomes, highlighting the importance of discussion with medical staff to come to an agreement on the specific target population. Akceso's recent experience in supporting orphan drug access negotiations confirms this.

Biosimilars ≠ generics

A key factor that might drive the use of MEAs is that biosimilars are not generics, and present different challenges,[xi] even though they are often grouped in policy documents. The potential for 'biobetters' highlights the difference between biosimilars and generics.[xii]

There is a remaining need to improve the regulations on interchangeability; to clarify the difference between substitutable and interchangeable. Europe is acknowledged to be much more advanced than the USA (with over 20 products approved in the last 20 years, v. only 2 currently approved), but there is still significant variation globally in approaches e.g. in China the biosimilar is the originator.

From an industry perspective, the specific challenges of commercialising biosimilars mean it can be difficult for an originator company to manage biosimilar launches – they are not used to seeing the price of high-value products dropping. Launching biosimilars requires an entrepreneurial and innovative mind set, with every market presenting different challenges.

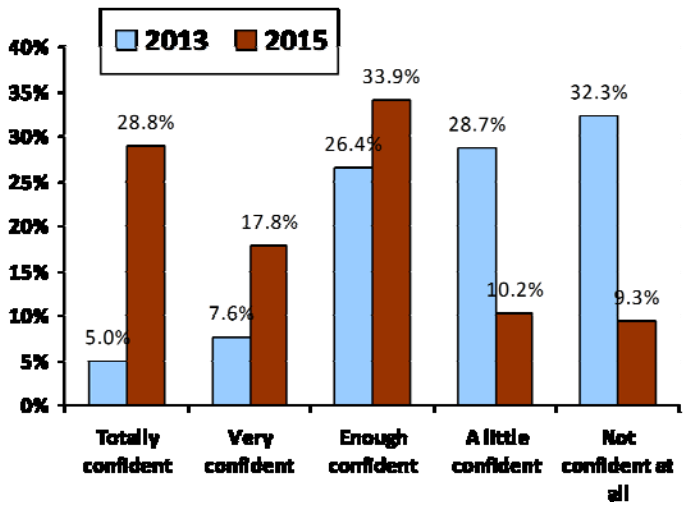
The continuing tangle of patent litigation in the USA[xiii] has produced a decision that may change one particularly challenging area for commercialising biosimilars. Biosimilars have required much more investment in Development than generics, with clinical trials that resemble Phase III studies for innovator drugs, even though this contradicts the concept of similarity.

Apotex recently submitted a citizen petition to the FDA against the small biotech Coherus, who are developing a biosimilar of pegfilgrastim without conducting a Phase III trial. The FDA had some other concerns about Coherus' plan, but did not express concern about the lack of a Phase III trial[xiv] - will this lead to a general reduction in the size of clinical trials conducted for biosimilars?

Improving Education: How do we increase confidence in biosimilars?

There is a clear need for increased efforts in educating payers and healthcare professionals about biosimilars. Hungarian physicians continue to mistrust biosimilars, whilst in Spain some doctors "still don't know what a biosimilar is". A recent study looking at opinions about biosimilars across the European Crohn's Colitis Organisation[xv] showed increasing trust in the EU, with only around 20% of interviewees feeling little or no confidence in their use in 2015, compared with 63% in 2013. This differs significantly with views in the USA, where levels of trust remain lower.[xvi]

European Crohn's Colitis Organisation Study



Source: ECCO survey, Danese S, Fiorino G, Michetti P 2016/JCC 2016

Mr Panaligan noted that providing education is a major part of commercialising biosimilars, not just 'selling'. The varied rate in adoption of filgrastim biosimilars is in part explained by the concerns that physicians still have about their safety. The Cancer Vanguard, a UK NHS organisation, has recently partnered with Sandoz and Amgen to create a set of tools to help educate healthcare professionals & patients.[xvii]

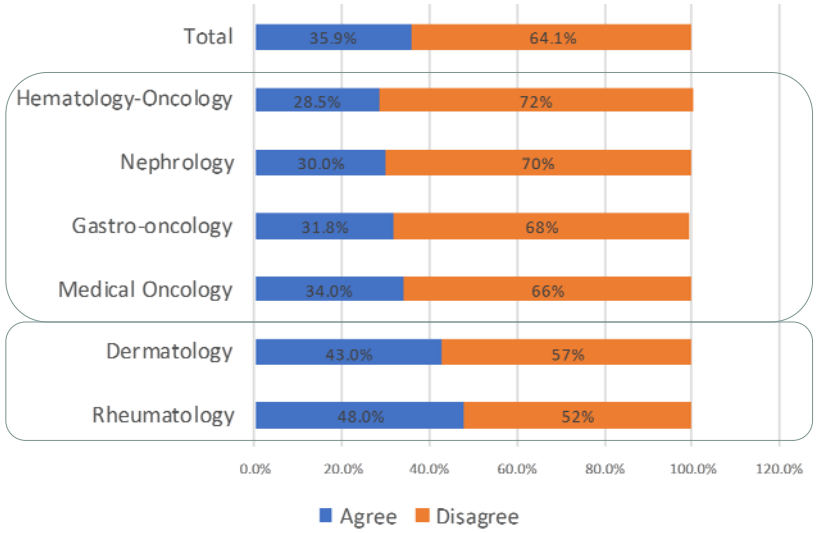
Other barriers to increasing adoption are the differences in usage policies from one country to the next, and the continuing payer focus on cost rather than value. Do hospitals assess the full 'cost-to-change' when considering switching to a lower budget impact biosimilar? This is an area where better analytics and modelling could help.

What's driving the pricing of biosimilars?

Payers appear to expect the same discounts for biosimilars that they have received for generics, but at current discount levels (apart from those imposed by law) are not generally reaching generic levels. Opinion suggests that bigger discounts will eventually emerge, but this could take 10 years.

The Phase III clinical trials currently conducted for biosimilars are expensive. Whilst appropriate evidence is of course required, trial costs, as well as the complexity of manufacturing and the need for an education-focused sales force, are barriers to companies readily providing generic-level discounts. Significant improvements in the use and acceptance of *in silico* development - modelling and analytics - could reduce the size (and thus the cost) of trials required to show equivalence to originators.

It is important to remember that existing biosimilars are based on high cost biologics, so even with cost savings they are still expensive drugs. It is clear that there need to be several competitors in a market to get real competition, and that perhaps infliximab might be a strong pathway to adopting biosimilars more widely. At present originators have not generally blocked biosimilars through price changes, but this remains a possibility.



Respondents were asked if they believe a biosimilar will be less safe than its originator biologic because is will be approved through an abbreviate pathway

Source: Cohen et al, Adv Ther DO! 10.1007/s1 2325-016-0431-5

Innovative biologics entering biosimilars space

With the current and upcoming wave of mAb biosimilars entering into different therapy areas such as oncology, musculoskeletal and central nervous system, new innovative biologics for the same conditions are facing payer-relevant comparators of biosimilars. To be able to command the reimbursed price levels their manufacturers target, the value proposition of new drugs needs to be clearly communicated to differentiate against existing treatments and their biosimilars. Market & patient access success requires a very customised approach, with Managed Entry Agreements structured to specific country conditions to achieve access.

What's the future for biosimilars?

We are still in an early phase of the biosimilars journey; very few companies have had success so far. Wave 1 has focused on the 'simple' biologics; the more complex drugs are expected to be the focus in Wave 2, bringing additional challenges.

The variance in adoption rates can produce situations where the first exposure in a country to a biologic is the biosimilar; the rise of biosimilars to become the 'new' Standard of Care at a lower price may be the tipping point for adoption. We also need to bear in mind that pharmaceutical therapy will continue to change over time, so it is likely that biosimilars will only be part of the overall range of therapeutic options.

Conclusions

Payer expectations of biosimilars seem to be déjà-vu of the early days of small-molecule generics: payers expect and promote strong price competition and would welcome at least 5 contenders for each molecule. While only a handful of markets with published price discounts for biosimilars v. original biologics (e.g. Norway) have reached levels similar to those of small-molecule generics, confidential discounts are believed to be very substantial in many European markets.

Novel compounds in therapy areas with biosimilars must provide strong payer-relevant value differentiators – clinical and economic – to commend the price levels their manufacturers target to be accessing the market and patient, or otherwise may not get reimbursed at those prices.

Andras Incze

Biosimilar entry is helping to rewrite treatment protocols, leading to increasing numbers of patients receiving these drugs. Payers are therefore challenged to maintain or even reduce related healthcare budgets while volumes are increasing, resulting in pressure on biosimilar net prices, even if list prices do not look heavily discounted.

BD&L executives conducting both in- and out-licensing need to consider all of the above issues when evaluating the potential market dynamics of an asset, to arrive at a robust due diligence assessment and ultimately a successful win-win deal.

References

[i] http://ec.europa.eu/DocsRoom/documents/7651/attachments/1/translations/en/renditions/pdf&usg=AFQjCNHF1O5abRKi-Vgl-q8PzEEMd0hOsg

[ii] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4323448/

[iii] https://static1.squarespace.com/static/579a1c55ebbd1a7a7dcc3645/t/57c61cc5e6f2e1b49dec8e3a/1472601286452/SSRN-id2812938+-+The+Impact+of+the+Entry+of+Biosimilars+-+Evidence+from+Europe.pdf

[iv] https://www.ohe.org/sites/default/files/849%20OHE-IHE%20executive%20report%20final%20Sept%202016.pdf

[v] http://www.bollettinosifo.it/articoli.php?archivio=yes&vol_id=2472&id=25858

[vi] https://kce.fgov.be/publication/report/barriers-and-opportunities-for-the-uptake-of-biosimilar-medicines-in-belgium

[vii] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360634/

[viii] https://structurecms-staging-psyclone.netdna-ssl.com/client_assets/dwonk/media/attachments/57dc/387d/6970/2d6c/ad6f/0000/57dc387d69702d6cad6f0000.pdf

[ix] http://www.lek.com/sites/default/files/1926_Asia_Biosimilar_adoption_manufacturing_Executive_Insights_a.pdf

[x] http://www.imshealth.com/files/web/IMSH%20Institute/Healthcare%20Briefs/Documents/IMS_Institute_Biosimilar_Brief_March_2016.pdf

[xi] http://www.europarl.europa.eu/RegData/etudes/STUD/2016/587304/IPOL_STU(2016)587304_EN.pdf

[xii] http://www.genengnews.com/gen-exclusives/biobetters-fulfilling-potential/77900863

[xiii] http://www.patentdocs.org/followon_biologics/

[xiv] https://www.thepharmaletter.com/article/amgen-s-gain-on-neulasta-no-consolation-to-coherus

[xv] https://www.ncbi.nlm.nih.gov/pubmed/27112706

[xvi] https://link.springer.com/article/10.1007/s12325-016-0431-5

[xvii] http://cancervanguard.nhs.uk/nhs-cancer-vanguard-working-to-make-better-use-of-cancer-medicines/