**INTRODUCTION**

The potential for biosimilar medicines to deliver high-quality treatment for a low price has long been recognised. Governments may realise savings through using biosimilars, meaning that resources can be used to treat more patients and purchase innovative therapies.

A manufacturer's decision to enter a market is determined by the presence of direct competitors. The price development of originator products is affected by the price development of biosimilar entrants locally. Governments may realize savings through using biosimilars, meaning that resources can be used to treat more patients and purchase innovative therapies.

**STUDY OBJECTIVES**

- To establish the direction of causality between the number of biosimilar competitors and biosimilar prices in the European market.
- To ascertain potential differences between biosimilars and experts in terms of entry choices.
- To estimate the impact of biosimilar prices on originator prices.

**METHODS**

An informed understanding of the price-dynamics in each market was obtained via a semi-structured literature review, as well as a survey and considered pilot with country experts (Figure 1).

Ten European countries were included in the analysis, in order to provide a comprehensive and diverse picture of the market access environment in Europe. Two International Nonproprietary Names (INNs) with successfully launched biosimilars were included: epoetin and filgrastim.

The period encompassed the years 2008 to 2016. The exploratory analyses rested on an econometric model with dynamic panel data analysis utilizing Ordinary Least Squares regression with fixed effects, subjected to a Granger causality test. The study aims to determine the number of biosimilar competitors and the number of patients in each market, as well as the market access environment.

The model of epoetin is dominated by the entry effect and biosimilars drive the number of competitors. The number of biosimilar competitors in the current market was less than 7% (p=0001) price decrease in the following month, with an long-run insignificantly sustained effect of 4% (L1,080).

As more competitors enter the market, the cohort of patients who are potential candidates for the medicinal product remains largely unchanged (abstaining from any possible change in disease incidence rates).

In order to serve the same patient population for a certain disease and to successfully gain market share, companies may need to differentiate their medications predominately through price – this effect is amplified by the fact that biosimilars are not directly substitutable and there are still many prerequisites as to their interchangeability.

Prices remain a main feature of differentiation between the separate biosimilars of epoetin, with the very nature of the product explaining why the number of competitors which influence the current market.

It is clear that for epoetin, the competition effect predominates, whereby each consecutive entrant has the power to drive prices down – this suggests that the epoetin market reaches saturation much faster, compared to the filgrastim market.

This is confirmed by the fact that, although seven products of the epoetin class have been granted marketing authorization in Europe, the market has fewer competitors locally (up to four), whereas for filgrastim the number can reach seven.

The faster market saturation for epoetin generally means that an optimal point of market participants has been reached sooner than it has been for filgrastim.

A possible explanation for the divergence in terms of direction of causality between biosimilars and experts in their molecular structure – more complicated INNs are not only more costly and difficult to manufacture, but carry a higher risk of immunogenicity.

**RESULTS**

**Relationship and direction of causality between number of biosimilar competitors and biosimilar prices**

The study assumes that the prices of currently marked biosimilars define the attractiveness of the market and the impact the entry decision of further competitors – in principle, the market of INNs is driven by two effects simultaneously:

- The entry effect, where higher prices attract more competitors.
- The competition effect, where an increase in the number of firms triggers a price reduction.

The market of filgrastim is dominated by the entry effect and biosimilars drive the number of competitors: the number of biosimilar competitors in the current month was less than 7% (p=0001) price decrease in the following month, with an long-run insignificantly sustained effect of 4% (L1,080).

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A possible explanation for the divergence in terms of direction of causality between biosimilars and experts in their molecular structure – more complicated INNs are not only more costly and difficult to manufacture, but carry a higher risk of immunogenicity.

This can increase doctors’ unwillingness to prescribe them, which slows down their market uptake, as well as the accumulation of real-life data concerning the clinical use of a biosimilar – this can potentially preclude biosimilar competitors from entering.

Given the molecular complexity of biosimilars of monoclonal antibodies (mAbs), the market dynamics governing their entry may more closely resemble that of experts rather than biosimilars.

**Effect of biosimilar prices on originator prices**

The relationship between biosimilar and incumbent prices is important because it indicates to what extent the originator may expect to sustain its market share by downward price adjustment, rather than by any other type of product differentiation.

This study has found a strong trend indicating that a tripling in the number of competitors leads to an approximate 18.5% increase in the number of competitors in the current month – this suggests that a potential increase in the current prices attracts more entrants.

The outcome is consistent with the fact that there are more approved biosimilars of epoetin in Europe compared to epoetin – i.e. compared with the market for epoetin, the market for filgrastim took a longer time to reach saturation.

**LIMITATIONS**

- This study used average manufacturer prices, which exhibit some variation throughout time.
- The averages contain several products of the same brand and those are sold in different formulations, which may occasionally cause additional fluctuation in the average prices due to the corresponding sales volume.
- This study has been conducted based on the visible Manufacturer Selling Prices, without accounting for hospital discounts on the market where filgrastim or epoetin are purchased by hospitals of other purchasing or procurement bodies.
- Findings would be strengthened by the inclusion of a regulatory parameter in the regression (e.g. a national policy which has been introduced in the recent years, such as the adoption of FPR for biosigis, the implementation of a mandatory price cut for originators or biosimilar entrants, the establishment of tendering as a standard means of procurement of biosigis, or another type of cost containment measure).

**DISCUSSION AND CONCLUSION**

The results from the present study inform the understanding of the causality of price erosion and market entry decisions for two INNs in Europe.

There have been convincing indications for cross-country differences with respect to number of biosimilar competitors – biosimilar manufacturers should carefully analyze the number of competitors planning to enter the market when making strategic decisions on the investment in the development of biosimilars.

On the market of filgrastim, the entry effect predominates, while on the market of epoetin, the competition effect holds the upper hand:

- A 3% increase in filgrastim biosimilar prices leads to a 38.5% increase in the number of competitors from one month to the next.
- Each next entrant would bring an approximate 7% decrease in the price-change rate of biosimilars of that product from one month to the next.
- Competition is not the single factor defining originators’ price decrease – for filgrastim, the model predicts that a long-term 10% price erosion is reached when the competitors have tripled in number.
- In reality, such price erosion can be reached much earlier – as such, it can be concluded that many of the drivers of price erosion remain in the hands of national authorities who exercise more leverage via regulations on biosimilar prices.

**REFERENCES**

1. Araneta, R., et al. (2014). “The potential for biosimilars to deliver high-quality treatment for a low price has long been recognised.” 3rd International Conference on Biologics and Biosimilars, Milan, Italy.