Biosimilars – the way forward

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Biotechnology represents a considerable opportunity, but also a challenge, given the complexities and risk associated with the development and manufacture of biological medicines

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In early 2004, the patent protection for several first generation biopharmaceuticals began to expire, opening the door to the so-called 'biosimilars'. The knowledge on biosimilars is steadily growing, and keeping up with state-of-the-art technologies and methods for protein characterisation is compelling, not only for manufacturers but also for the authorities. The challenges now are to review current marketing approval procedures and to develop standardised methods for evaluating the quality, safety and efficacy of these products.[1]

It is worth noting that a wide range of biosimilars have been sold for many years in several unregulated markets of Asia, Eastern Europe and Latin America. Examples of such marketed products include: interleukins, interferons, erythropoietins, growth factors, hormones, enzymes and monoclonal antibodies.[2] However, it is the valuable Western market that is raising the most interest in the biosimilar sector.

Clinicians need to be aware of the important issues surrounding the use of biosimilars. Greater awareness of the potential differences between products will enable clinicians to make informed prescribing decisions, which are critical for patient safety.[3] Entry of biosimilars into the market requires transparency and impartial information for both health professionals and patients.

As experience with the first biosimilars products is gained, current EMEA guidelines for biosimilars marketing approval will be reviewed to cover the latest advancements and also new guidelines will be created for new classes of biosimilars.

Biotherapeutics account for 7.5% of all drugs on the market, comprising approximately 10% of the total expenditure for marketed drugs, and their use is growing exponentially at more than 20% per year. Biotechnology drug candidates constitute 32% of all pipeline research programs.[4]

This projected market growth along with the fact that several 'blockbuster' biopharmaceuticals have reached, or are reaching, the end of their patent protection is attracting biosimilar firms into the market.

A number of biosimilars are already approved and others are under development. There is no doubt that these drugs will play an important role in healthcare. Despite the fact that biosimilars provide a number of opportunities, it is important that they are introduced in an appropriate manner.[5]

Key market drivers and barriers

Biosimilars development is currently underway across all product classes that fall under the category of recombinant proteins (EPOs, granulocyte colony stimulating factors 'G-CSFs', insulins, growth hormones, interferons, etc). The vast majority of these drugs were approved during the 1980s, and their patents have expired over the past years, creating a significant commercial opportunity for biosimilar manufacturers.[6]

The key growth drivers for the biosimilar market are the rapid growth in the biologics field, the patent expiration of several biotech "blockbusters"; technological advances enabling a better characterisation of biologics obtained from different manufacturing processes; cost containment pressure from health systems and the regulatory pathway established in Europe.

The current trends indicate that the resources required for biosimilar development create high barriers for entry not just to the small companies but even the larger generics and biopharmaceutical companies. The cost and complexity of the development process for biosimilars, the lack of automatic substitution of branded products and the defensive strategies being employed by innovator companies are factors that slow down the entry to the biosimilars market.

The biosimilars manufacturers have to put more trust in the Clinical Research Organisations (CROs), which help them to design appropriate preclinical and clinical studies (focus on correlating comparability to the reference product). Furthermore they help to develop a long-term pharmacovigilance plan in order to prove that their biosimilar has the same clinical properties and it is as safe as the innovator medicine.

Therefore, the market may develop slowly, which is one reason why the commercial rewards are likely to be limited in the short term.

Biosimilar products will compete with originator biologicals, many of which already compete with other originator brands made by different biotech companies. But in many cases, biosimilars are copies of older

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biological medicines, for which second-generation biological medicines are already available. This means that the biosimilar products will mainly compete with each other and the older biological medicines rather than with the most recent treatments developed by originator companies, which can offer increased therapeutic benefit to patients.[7]

Regardless of competition from biosimilars, the market for first generation biologics is expected to fall after 2010 as new second generation products enter the market. Only interferon beta and human growth hormones are expected to obtain accelerating sales growth in the period to 2010 as consequence of the lack of competition from the before commented second generation products.

Cost savings

Biopharmaceuticals are more expensive than small-molecule drugs, and their use is increasing. An important benefit of biosimilars is that they are associated with cost savings, but currently not as much as with the generic drugs (80%).

According to figures by the European generic association (EGA), generic medicines have made a major contribution to affordable and accessible healthcare for over 20 years, saving the European Union (EU) alone an estimated €20 billion annually.[6]

However, smaller cost savings, perhaps in the region of 15–30% off the cost of an originator protein, can be significant. Further savings would be possible if it was not for the high development costs for the complex manufacturing processes and analytical methods, as well as costs related to the mandatory comparative clinical trials to show comparability.

This more cautious saving should not discourage the enthusiasm for facilitating the approval of safe and effective biosimilar products.[8]

In the short term it is unclear how cost pressures from biosimilars will affect the prices of innovative products. Manufacturers may alter pricing strategies prior to patent expiration to help them recover their investment costs. Nevertheless, cost savings with biosimilars will likely increase access to therapeutic proteins and stimulate innovative research.[5]

The potential savings for healthcare providers and consumers is potentially a key driver of demand for biosimilars. Currently, the high costs of treatment with protein therapeutics creates a significant tension on healthcare providers. Therefore these providers are expected to create incentives for the use of biosimilars.

The speed with which they adopt biosimilars and start restricting reimbursement for branded drugs will depend on the clinical experience with biosimilars, especially their safety profile. Therefore a time gap is expected between the marketing approval of a biosimilar and its acceptance by healthcare providers.

Conclusion

Not a week seems to go by that doesn't show news of a large pharmaceutical company announcing plans to "become more biotech-like" or making moves to partner with biotechs and more importantly to make use of the benefits of biologics technology to revive its own pipelines.

Biotechnology represents a considerable opportunity, but also a challenge, given the complexities and risk associated with the development and manufacture of biological medicines.

Biosimilars are unlikely to result in the same price competition as has occurred with generic medicines. The pricing strategy for each biosimilar will need to balance two forces:

- The price will have to reflect the high investment in development and manufacturing. The cost savings will not be as large as some have estimated (15–30% off of the cost of an originator protein).
- A small price differential reduces the incentive to switch. Health professionals will be cautious about the safety and efficacy of biosimilars in the short term at least.[9,10]

Biosimilar drugs have a significant market share that has already started to generate revenues and push the industry toward overall profitability. This trend shows signs of longevity. ■

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