Introduction of biosimilars: not to be confused with generics

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Generic versions of branded medicines have been with us for a long time – there was a proliferation of generic versions of aspirin, for example, when Bayer’s patent expired in 1917.1 We will all be familiar with the process through which generics are introduced to the market: the originator brand product has a finite patent life, at the end of which other manufacturers can apply for a licence to manufacture and market a generic version.

Production of generic medicines is reasonably straightforward for synthetic chemical drugs, in which the active substance in the generic medicine is identical to the active substance within the originator brand. While there may be some small differences with respect to excipients used in generic formulations, to all intents and purposes generic medicines are the same as the original brand.

So when is a generic not a generic?

A generic isn’t a generic when it’s a biological drug. Biological drugs (biologics) are, generally, large molecules based on sugars, proteins, nucleic acids or complex combinations of these substances, and are produced through complex biotechnological processes rather than being chemically synthesised.

Since the follow-on manufacturer does not have access to the originator’s molecular clone bank and original cell bank, they cannot guarantee that their version is exactly identical to the original manufacturer’s version (known as the biological reference medicine).

Unlike synthetic chemical drugs, there may be significant differences between the biosimilar and the biological reference medicine in terms of efficacy or adverse effects.2 In addition, since biologics are administered parenterally, biosimilars may require different delivery systems from the reference medicine.

In the EU a specially adapted approval procedure has been introduced for certain biologics, termed similar biological medicinal products – shortened to biosimilars. This procedure is based on a thorough demonstration of ‘comparability’ of the biosimilar to the biological reference medicine. This procedure is more rigorous than for small-molecule drugs proven to be identical to each other, but less testing than for completely new drugs.

Unlike generics, new biosimilars have black triangle status at the time of initial marketing. It is therefore important to report all suspected adverse reactions to biosimilars using the Yellow Card Scheme (refer to the Medicines and Healthcare products Regulatory Agency website). For biosimilars, adverse reaction reports should clearly state the brand name and the batch number of the suspected medicine.

Implications for health systems

The health systems in the UK have a long history of successful introduction of generics. Pharmaceutical companies know that they have a limited window within which to maximise profits from their products before patent expiry, after which generics will almost inevitably be introduced at much lower prices, thereby providing the NHS with windfall savings.

Those of us who work within the NHS as well as those in the pharmaceutical industry all know the game. The rules may have changed slightly over the years, but the basics are the same: NHS advisers will push for maximum use of generics, while industry will push the claims of superiority for their branded products. Generally the first, or in many cases the second, drug of a new class will establish itself as class leader and any subsequent drug in the same class will be viewed as a ‘me-too’ and may struggle to establish anything other than a small niche in the NHS market.

Later entrants to the market will offer lower prices to try to compete with the market share of the first couple of drugs, often with minimal success, although in some cases improved clinical effectiveness may enable later entrants to establish a larger market share.

Use of generics provides benefits to patients and the NHS, not least of which is the fact that the lower price increases overall access to effective medicines. So generic versions of very expensive medicines, such as biologics, would be welcome. Unfortunately, due to the reasons outlined above, true generic versions of biologics will not be produced. We are, therefore, faced with the introduction of a range of biosimilars.

Unlike with true generic medicines, where clinical data for the originator product will hold true for the generic, clinical evidence for each biosimilar will have to be assessed individually. Therefore, it would be inadvisable to switch patients from the agent on which they have been established to a biosimilar in order to save money on acquisition costs. Biosimilars will need to be introduced in a safe and measured way, eg using them in newly diagnosed patients and in patients needing to change therapy.

The good news for patients and the NHS is that manufacturers of biosimilars will seek to maximise benefits of their product and may introduce new administration systems or provide patient support programmes not offered by the originator company, so there may prove to be benefits to both patients and the NHS from the careful introduction of biosimilars.

Conclusion

We need to be cautious and remember that biosimilars are not generics and should be treated as new drugs. Biosimilars may
prove to be bio-better or bio-worse: only time will tell for each individual product.

References

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