HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Outcome of the Process - Public Consultation on the Update to the Guide to Biosimilars for Healthcare Professionals

1 INTRODUCTION

The public consultation on the update to the HPRA Guide to Biosimilars for Healthcare Professionals was closed on 23 December 2019. Inputs to this consultation continued to be received and were accepted after this date. The HPRA would like to thank everybody who contributed to the process. Below is a document summarising the outcome of the consultation process.

The guide is intended to provide information on the regulation of biosimilar medicines in Ireland. The guide is targeted primarily at healthcare professionals but is also relevant to manufacturers and distributors. Four years have passed since the Guide was published; in that time the use of biosimilars across the EU has grown considerably and more data on their use is available. Therefore, the guide was updated to reflect the current state of knowledge. The draft updated guide was open for public consultation to gather feedback from stakeholders, in particular to get feedback on the proposed changes to the text on interchangeability and switching. The content of the guide has been amended to take account of the comments received, as appropriate.

2 NUMBER OF RESPONSES

During the public consultation process, the HPRA received responses from a range of stakeholders including the Irish Pharmacy Union (IPU), hospital pharmacists, regulatory affairs professionals, industry bodies including the Irish Pharmaceutical Healthcare Association (IPHA) and Medicines for Europe, and a range of marketing authorisation holder companies. The HPRA welcomes all the suggestions and contributions made, and while we were not always able to take on board the proposals, we would hope that this document provides an explanation for our approach.

2.1 Summary of responses received

Comments were received on several sections of the Guide, with the majority of comments focusing on the interchangeability, switching and prescribing section. In general, the comments supported updating the guide. Several editorial comments resulted in improvements to the readability of the text, but are not discussed in detail here.

Representatives of the pharmacy profession welcomed the update and considered that it addressed the changes in the biosimilar space, which have taken place since the previous version was published. It was suggested that the HPRA consider updating the text of the guide to allow pharmacists to switch patients from a biological reference medicine to a biosimilar.

Industry stakeholders highlighted that more emphasis should be placed on the variability of biological medicines and, in particular, that it is not possible to demonstrate that a batch of any biological medicine is identical to previous batches. In addition, it was felt that more emphasis could be placed on the fact that quality testing and molecular characterisation represents the cornerstone of establishing biosimilarity, as this concept may not be fully appreciated by physicians. Industry stakeholders also recommended introducing more descriptive text on how extrapolation is underpinned by the comparability exercise.

Industry stakeholders supported the role of the physician in biosimilar switching. However, the frequency of switching was highlighted as an issue for reasons of traceability, patent confusion and changes to patient support services. It was suggested that the guide should limit the number of switches that are permissible. Several comments focused on switching between biosimilars and highlighted the fact that there are no clinical studies addressing biosimilar-to-biosimilar switching. It was also suggested that the guide should include a regulatory policy position which addressed the risks of automatic substitution. Comments were received both for and against including reference to the HSE's Medicines Management Programme and the Best-Value Biological (BVB) programme.

Regarding pharmacovigilance and traceability, it was suggested to clearly emphasise that biologicals should be prescribed by brand name and that traceability to the batch number should be recommended in the case of any adverse drug reactions. Greater clarification relating to the specifics of how to prescribe biosimilars was also requested.

A comment on the summary of product characteristics (SmPC) for biosimilar medicines stated that biosimilar labelling should include data and information about the reference product and the biosimilar itself.

3 HPRA RESPONSE

3.1 Updates following the consultation

The HPRA has on taken board the comments and suggestions received during the consultation across all areas. Throughout the document, several welcome editorial suggestions were accepted, as they improve the readability of the guide. The key changes made to the Guide as a result of the public consultation are discussed below, as well as explanations for why some requested changes were not implemented.

As suggested, the natural variability of biological medicines has now been highlighted in the revised text and it is emphasised that, for biological medicines, no batch is truly identical to previously manufactured batches. More emphasis has also been placed on the fact that physiochemical, molecular and biological tests are more sensitive than clinical studies in detecting any potential differences. The scientific underpinning of extrapolation has been stated in a clearer fashion, including the scientific bridge provided by the combination of analytical testing and relevant non-clinical and clinical studies.

Regarding interchangeability and substitution, it is recognised that there is a desire from pharmacists to introduce pharmacy-lead substitution. However, the scope of the Guide is consistent with the provisions of the Health (Pricing and Supply of Medical Goods) Act 2013, which currently excludes biological medicinal products from the list of interchangeable medicinal products. Therefore, the text was not updated in this regard.

Regarding the frequency of switching and biosimilar-to-biosimilar switching, no changes were made to the text. The HPRA considers that once approved, biosimilars are considered interchangeable and switching studies are not a regulatory requirement. There is no evidence to substantiate a cautionary statement on repeated switching or switching between biosimilars. Therefore, the guide does not distinguish between originator-biosimilar switching and biosimilar-biosimilar switching. Indeed, as already stated in the guide, the EMA defines interchangeability as the 'possibility of exchanging one medicine for another medicine that is expected to have the same clinical effect. This could mean replacing a reference product with a biosimilar (or vice versa) or replacing one biosimilar with another'. Therefore, the nature and frequency of any switching is a matter for prescribers and patients. In addition, the support services that individual companies may offer is considered to be outside the scope of this guide.

The proposal to reference specific HSE guidance documents generated divergent views. The HPRA has considered this further and the guide now states more generally that further information on prescribing in the context of switching may be accessible from the HSE.

Industry stakeholders suggested that patient consent should be specifically referenced in the updated guide. However, discussions between prescribers and patients fall within the remit of clinical practice and therefore are not within the scope of this guide. The HPRA has published a separate questions-and-answers document for patients.

No updates were made to the labelling requirements for biosimilars; the content of the SmPC for biosimilars is an EU-wide decision and therefore cannot be addressed in the current guide.

The HPRA recognises that prescribing of biologicals by brand name is important for traceability. Further text has been added, highlighting that biologicals should be distinguished by trade name. Furthermore, the text has been updated to recommend the recording of the batch number in the event of an adverse drug reaction.

4 CONCLUSION

There was a broadly positive response to the update to the HPRA Guide to Biosimilars for Healthcare Professionals. Many informative comments and suggestions were received and these have been largely considered in the finalised guide. We would like to thank all those who contributed to the consultation process.

Human Products Authorisation and Registration Department