NATIONAL ORGANISATION OF MEDICINES (EOF)

CIRCULAR

Ref. no. 126908/12.12.2018

Having regard to:

1. Regulation (EC) 726/2004;

2. The guidelines of the European Medicines Agency (EMA):

EMA/CHMP/437/04 Rev 1 (23.10.2014): Guideline on similar biological medicinal products

EMEA/CHMP/BMWP/42832/2005 Rev 1 (18.12.2014): Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: non-clinical and clinical issues

EMA/CHMP/BWP/247713/2012: Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance - quality issues

3. Document EMA/940451/2011of the European Medicines Agency:

Questions and answers, 5 May 2011

4. Law 1316/1983, as currently in force;

5. Ministerial Decision 32221 (Government Gazette B 1049/29.04.2013);

6. EOF Board Decision O-275/13th/18.11.2018;

We hereby update information on biosimilars as follows:

A biosimilar is a biological medicine highly similar to another already approved biological medicine (the “reference medicine”) in terms of structure, biological activity, efficacy, safety and immunogenicity.

Biosimilars are not the same as generics, because the volatile nature of biological medicines and the complexity of their production process do not enable their accurate reproduction.

The differences identified between the reference product and the corresponding biosimiliar are minor, do not affect the quality or the activity of the medicine and are of no clinical relevance for the safety and efficacy of the medicine.

The EU Regulatory Framework on biosimilars has been in force since 2005. A key tool for the development and reliable assessment of the similarity between two biological products is a comparability exercise, which is a stepwise process covering all stages of development and is aimed to exclude differences in clinical performance between the reference product and it's the biosimilar under assessment.

Available pharmacovigilance data - over 10 years for the first biosimilars and 5 years for the first biosimilar monoclonal antibodies - complement and confirm the reliability of the European regulatory framework on biosimilars. From these data, along with a growing number of completed post-approval clinical trials, the following emerge with regard to the use of biosimilars:

- Biosimilars are as safe and effective in all their approved indications as the respective reference products, therefore
- The administration of biosimilars to first-time treated patients is acceptable, following a prescription by the attending physician and after the patient has been informed.
- The substitution between a biosimilar and a reference product, i.e. a change of treatment from the reference product to a biosimilar and vice versa, for a patient already being treated with a biological medicine is acceptable, following a prescription by the attending physician and after the patient has been informed.
- In all cases it is necessary to comply with the pharmacovigilance instructions applicable to all biological products: registration of the trade name and batch number of the medicine administered to the patient, in order to ensure that the report of any undesired affects can be with absolute certainty attributed to the product administered each time.

This Circular updates and replaces any previous relevant document.

The President of EOF

Aikaterini Antoniou

APPENDIX

- **EUROPEAN MEDICINES AGENCY (EMA)**

  https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines

Approved biosimilars in the EU

https://www.ema.europa.eu/en/medicines/field_ema_web_categories%253Aname_field/Human/ema_group_types/ema_medicine/field_ema_med_status/authorised36/ema_medicine_types/field_ema_med_biosimilar/search_api_aggregation_ema_medicine_types/field_ema_med_biosimilar

EU INFORMATION DOCUMENTS

http://ec.europa.eu/DocsRoom/documents/26643

https://ec.europa.eu/docsroom/documents/22924/attachments/1/translations/en/renditions/native

- **POSITIONS OF NATIONAL REGULATORY AUTHORITIES**

  BELGIUM:
  https://www.famhp.be/en/human_use/medicines/medicines/MA_procedures/types/Biosimilars

  DENMARK: https://laegemiddelstyrelsen.dk/en/sideeffects/biological-and-biosimilar-medicinalproducts/frequently-asked-questions

  FINLAND:
  http://www.fimea.fi/documents/542809/838272/29197_Biosimilaarien_vaihtokelpoisuus_EN.pdf

  GERMANY: https://www.pei.de/EN/medicinal-products/antibodies-immunoglobulins-fusion-proteins/monoclonalantibodies/biosimilars/position-pei-interchangebility-biosimilars-content.html

IRELAND: http://www.hpra.ie/homepage/about-us/publications-forms/guidancedocuments/item?id=e6d50326-9782-6eee-9b55-ff00008c97d0&t=/docs/default-source/publicationsforms/guidance-documents/guide-to-biosimilars-for-healthcare-professionals-and-patients-v2

ITALY: http://www.agenziafarmaco.gov.it/sites/default/files/Secondo_Concept_Paper_AIFA_BIOSIMILARI.pd f

NORWAY: https://legemiddelverket.no/nyheter/switching-between-a-reference-product-and-a-biosimilar

- **WORLD HEALTH ORGANIZATION (WHO)**
  http://www.who.int/biologicals/biotherapeutics/similar_biotherapeutic_products/en/11