15.5.3 Interchangeability and Substitution

In the EU, recommendations on interchangeability (i.e., the choice of a particular drug between two or more available for the same indication) and substitution (i.e., administrative rules that allow the switch from one medicine to another), either between innovative products or between innovative and biosimilar medicines, are under the remit of national authorities and outside the responsibility of the EMA and, therefore, have never been included in the guidelines on biosimilars.

Automatic substitution (i.e., switch from one medicine to another done at the dispensing level) is possible for the majority of generic medicinal products, therefore, this issue has also been widely raised for biosimilars even before they were available. Unlike generic drugs, the automatic replacement is not considered appropriate for biological medicinal products, and in many EU member states this has been stated through specific regulation (Ruiz and Calvo, 2011). This issue is still highly controversial, and, based on the experience gained in the use of biosimilars, some regulatory authorities have recently expressed opinions in favor of interchangeability and substitution for biosimilars (GaBI Online, 2015d).

The Dutch Medicines Evaluation Board (MEB) has reviewed their position on biosimilars (from 2010) to acknowledge that biosimilars have no relevant differences compared to an innovator biological medicinal product regarding quality, safety, and efficacy. In their initial opinion, patients must be kept on a biological medicinal product as much as possible if their clinical response was good and should not be switched to an equivalent biological medicine. If a switch was considered, it should only occur under strict conditions including the attending physician's approval. MEB's current position on biosimilars is a bit more relaxed, though still cautious about exchange between biologicals (whether originators or biosimilars) and emphasizing critical aspects of adequate clinical monitoring, pharmacovigilance and traceability, and the involvement of physicians and (hospital pharmacists) in any decision on switching between biological treatments.

An interesting experience on switching is currently taking place in Norway where large savings are expected after the acquisition of infliximab biosimilar Remsima through a national tender for biologics for rheumatology, and stomach, intestinal, and skin diseases in February 2015. Although patients being treated with the originator Remicade are expected to continue with their treatment, a clinical trial is under way in which patients will be switched from the originator Remicade to biosimilar Remsima in order to support the uptake of the biosimilar infliximab and to provide reassurance that switching between the originator and biosimilar is safe.

Recently, Australia's Pharmaceutical Benefits Advisory Committee (PBAC) also reviewed its previous position regarding substitution between the originator medicinal product and biosimilars. At its April 2015 meeting, it recommended that biosimilars are suitable for substitution at the pharmacy level where the data are supportive of this conclusion (GaBI Online, 2015e). Relevant considerations for this substitution are no significant differences in clinical efficacy or safety compared with the originator, no identified populations where the risks of using the biosimilar are disproportionately high, data to support switching between the originator and the biosimilar, and data for treatment-naïve patients initiating on the biosimilar.