

## **Biosimilar granulocyte-colony stimulating factor (G-CSF) for stem cell mobilization in related and unrelated donors**

Biological products such as granulocyte-colony stimulating factor (G-CSF), erythropoetin, interferons and many others have revolutionized the treatment of patients with cancer. The recent and pending patent expirations for a number of biopharmaceuticals have prompted the study and development of alternative versions of biological products referred to as biosimilars. Unlike generics of small molecules that are considered identical to the reference product, biosimilars are drugs similar but not identical to the innovative drug, characteristics of which are closely related to the manufacturing process. Guidelines for approval of biosimilars have been issued by the EMEA and vary according to the product. In general, the approval of biosimilars is based on the demonstration of equivalent efficacy and safety to the innovator product in comparative studies. In the case of G-CSF, equivalence has to be demonstrated in the prophylaxis of severe cytotoxic chemotherapy-induced neutropenia and extrapolation of efficacy to the other indications of the reference product (e.g. mobilization of stem cells) is then allowed. Because there is a limited clinical database on approval of a biosimilar (500-600 patients app.), pharmacovigilance is becoming essential, particularly as only six-month follow up is needed for safety in registration studies.

Considering the limited experience with G-CSF biosimilars and the extrapolation process for approval in less common indications, we feel that the use of biosimilars for stem cell mobilization and collection in healthy donors presents an ethical dilemma. Since healthy donors receive no therapeutic benefit from the receipt of G-CSFs for stem cell mobilization, ethical concerns dictate that drug safety is of paramount concern for these individuals. Considering the detrimental effect that unexpected toxicity might have in normal individuals, sufficient experience with the biosimilar product and adequate follow up should be required. Therefore the EBMT recommends evaluation of efficacy and safety data for stem cell mobilization before using biosimilar G-CSF in healthy donors. This can only be obtained by performing clinical trials with an adequate number of stem cell mobilization procedures with adequate follow up in autologous conditions. Until studies have been performed to provide the required efficacy and safety data, the EBMT does not recommend the use of biosimilar G-CSFs for mobilization of stem cells in healthy donors for stem cell transplantation.

Sincerely,



Dietger Niederwieser  
President of the EBMT on behalf of the Executive Committee