INTRODUCTION

Biosimilars and biobetters are subsequent versions of licensed innovator biotherapeutics. Biosimilars are designed to be similar to an approved originator biologic product, and are expected to demonstrate comparability to the originator product in terms of quality, safety and efficacy; whereas biobetters incorporate intentional modifications to the originator molecule profile with the aim of producing an improved product.1 This distinction between biosimilars and biobetters has important implications from a regulatory perspective, with biosimilars following class-specific guidance whereas biobetters are considered innovator drugs. Filgrastim, which is recombinant granulocyte-colony stimulating factor, is a biopharmaceutical drug for which there are biosimilar products.3 Within this product class are also two products referred to as ‘biobetters’ - pegylgrastim and lipegfilgrastim, which are pegylated forms of filgrastim.4,5 These pegylated forms are long-acting versions that require a lower frequency of administration compared with originator filgrastim.6

The regulatory approval of filgrastim biosimilars requires the demonstration of similarity to the originator.4,5 The specific non-clinical and clinical requirements are detailed in the guidance provided by the European Medicines Agency (EMA) for the development of similar biological medicinal products containing recombinant human G-CSF.3 Biosimilar filgrastim were granted European marketing authorisation based on demonstration of clinical comparability to the originator filgrastim Neupogen® in one indication (reduce duration of neutropenia and occurrence of febrile neutropenia in chemotherapy patients showing cytotoxicity), and extrapolation of the results to all five approved indications. The EMA guidance on biosimilars is not applicable to modified ‘biobetter’ versions of the drug, such as the pegylated forms of filgrastim. Pegfilgrastim (Neulasta®) demonstrated clinical non-inferiority to originator filgrastim in the same indication as above and was approved solely for this indication. The subsequently developed lipegfilgrastim (Lonquex®) was approved for the same indication but used pegfilgrastim as the comparator in clinical trials.

Decision drivers identified in the HTA appraisals were (Table 1):

France:3 The biosimilars were judged to have equivalent efficacy to the originator filgrastim and were placed in the category of no improvement in medical benefit (ASMR = 5). For the pegylated forms of filgrastim, although there were no improvements in terms of efficacy or safety with respect to filgrastim, the biosimilars were noted to have convenience of dosing as the primary driver leading to a positive recommendation for pegfilgrastim. However, for lipegfilgrastim, an increased risk of mortality in a subgroup of patients was noted, which is being evaluated further in post-marketing studies, resulting in the decision to not recommend in light of the availability of alternative drugs in this product class.

Netherlands:2 Similarity to the originator as judged by the EMA was accepted as sufficient evidence for the biosimilars and pegfilgrastim to be placed on the reimbursement list (Annex 1A). The pegylated forms were not assessed for comparability and were placed in the category of no improvement in medical benefit (ASMR = 5). Lipegfilgrastim was added to this reimbursement list, allowing for interchangeability of the originator filgrastim, biosimilar filgrastim, and the pegylated filgrastim product cluster on the GKV formularies.

Scotland:10 Evidence of clinical non-inferiority to the respective comparator was accepted in the appraisal of biosimilars and the pegylated forms of filgrastim. Economic evidence considered for the biosimilars consisted of a cost-minimisation analysis and a budget impact analysis, cost effectiveness data being directly comparable to the originator. The pegylated forms of filgrastim were considered beneficial in terms of convenience, with cost savings due to lower drug acquisition costs, and recommended for reimbursement. For lipegfilgrastim, a long-acting G-CSF is considered appropriate in line with current clinical practice.

REFERENCES


