REVIEW ARTICLE

Biosimilars in rare diseases : a focus on paroxysmal nocturnal hemoglobinuria

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Supplementary Information

Table S1: Key biosimilar definitions

Term	FDA definition	EMA definition
Biosimilar	A biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product.	A biological medicinal product that contains a version of the active substance of an already authorized original biological medicinal product (reference medicinal product) in the European Economic Area.
Extrapolation	The justification underlying "approval for other indications that were not directly studied by the biosimilar manufacturer." This is based on the totality of evidence supporting "biosimilarity [to] at least one of the reference product's indications," combined with "knowledge and consideration of various scientific factors for each indication," including "MOA, PK, PD, efficacy, safety, and immunogenicity."	Extension of the efficacy and safety data from a therapeutic indication for which the biosimilar has been clinically tested to another therapeutic indication approved for the reference medicine. Important considerations need to be borne in mind before an indication for a biosimilar can be approved based on extrapolated safety and efficacy data. These include a shared MOA and relevant study population.
Interchangeability	A biosimilar product that meets additional FDA requirements, including information showing that it is "expected to produce the same clinical result as the RP in any given patient."	Refers to the possibility of exchanging one medicine for another medicine that is expected to have the same clinical effect.

FDA, United States Food and Drug Administration; EMA, European Medicines Agency; MOA, mechanism of action; PD, pharmacodynamics; PK, pharmacokinetics; RP, reference product.

Figure S1. Critical quality attributes of a monoclonal antibody biosimilar[11]