

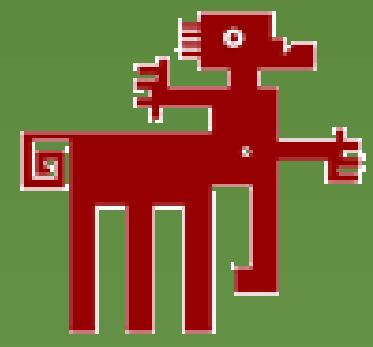
Regulatory viability of biosimilars in veterinary medicine



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Introduction

Biological medicines have revolutionized the treatment of a broad spectrum of diseases. In spite of their therapeutic value, the cost of those products is threatening the sustainability of healthcare systems. Regulators have opened the possibility of developing lower cost versions of those original biologicals used in humans; the so-called **biosimilars**. Can a biosimilar of a veterinary medicine be developed, and how should it be studied? The **main objectives** are: **a)** identify and select a biomedicine of veterinary-use product as a reference medicine for development of a biosimilar candidate, and **b)** suggest the experimental studies needed to develop a biosimilar in veterinary medicine.

What are biosimilars

Biological drugs are produced in living cells. A biosimilar is a biological medicinal that contains a version of the active substance of an already authorised original biological medicine the patent of which has already expired. Any difference with the original product should not compromise safety nor efficacy.

Regulatory framework

Demonstration of biosimilarity is based on a comprehensive comparability exercise. It includes analytical structural and analytical comparability, the cornerstone of biosimilarity, non-clinical studies, bioequivalence, and studies in patients. If approved both active substances can be considered essentially the same, and they may be given via the same route, the same posology and for at the most the same indications. The European Medicines Agency lead the issuance of a regulatory framework, and was followed by major agencies.

Physicochemical trials

Functional *in vitro* and/or *in vivo*

Non-clinical toxicity studies

Clinical studies

Development proposal of a biosimilar of lokivetmab

Primary structure (identical)

HOS compared evaluation

Glycoprofile and disulphide bonds

In the light of the principles guiding human biosimilars development, set studies is proposed to demonstrate biosimilarity between the candidate and lokivetmab.

Antigen binding kinetics comparison (Biacore) and *in vitro* bioassay

Clinical pharmacokinetics and pharmacodynamics comparison (models)

Conclusions

Lokivetmab is an ideal candidate from the scientific and the market perspective to be used as a reference product for biosimilars development. It may rise investors interest.

Lokivetmab biosimilar development plan may not necessarily include trials in patients. A heavy structural and functional comparability may strongly reduce the need for a clinical phase.

Advantages and interest of biosimilars

They may prevent supply shortages of biological medicines.

Through competition they provide increase access of patients to buy them.

They contribute to National Healthcare Systems sustainability.

They may contribute to innovation: new drugs are developed to overcome biosimilar competition, and the resources may be redistributed to new drugs acquisition.

Biosimilar candidate: lokivetmab

Lokivetmab (active substance of Cytopoint) is a fully caninised monoclonal antibody (mAb) of the IgG class authorised for the treatment of chronic manifestations of atopic dermatitis in dogs. Being a highly characterised biopharmaceutical product, approved for the treatment of an increasing prevalence disease and with a remarkable safety and efficacy profile, it's a suitable product as a reference medicine for the development of a biosimilar candidate.

	Generics	Biosimilars
Source	Chemical synthesis	Produced in a living system
Molecules	Small and easy to characterise	Often molecules bigger and structurally more complex
Authorisation	National	Centralised by EMA
Drug development timeline	2-3 years	6-7 years
Clinical trials	Bioequivalence in healthy volunteers	Preclinical and clinical trials in patients
Toxicologic studies	No	Yes
Pharmacovigilance	Normal	Special
R+D costs	0,6-4 million €	50-150 million €

Table 1. Comparison of development and characteristics between generics and biosimilars.

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