Environmental Risk Assessment Summary
Mosunetuzumab

Introduction

The publication of environmental risk assessment summaries is part of Roche's engagement on developing a better understanding of issues regarding pharmaceuticals in the environment (PiE).

New pharmaceutical substances are investigated for biodegradability and initial ecotoxicity during their development. For registration, a full state-of-the-art environmental risk assessment is developed based on chronic environmental effects and advanced environmental fate data, as required by the pertinent regulations. While not a regulatory requirement, Roche also investigates older pharmaceutical substances, normally at a simpler scale, in order to assess their environmental risks.

The EMA Guideline on Environmental Risk Assessment (ERA) for Non-GMO Human Medicinal Products [4] requires an ERA for the Marketing Authorisation Application (MAA) of all new medicinal products in the European Union. For proteins and peptides, however, the 'ERA may consist of a justification for not submitting ERA studies, e.g., due to their nature they are unlikely to result in a significant risk to the environment'.

Summary

Mosunetuzumab is a recombinant bispecific antibody for the treatment of adult patients with relapsed or refractory (R/R) follicular lymphoma (FL). It is a first-in-class CD20xCD3 T-cell engaging bispecific antibody designed to target CD20 on the surface of B-cells and CD3 on the surface of T-cells. This dual targeting activates and redirects a patient's existing T-cells to engage and eliminate target B-cells by releasing cytotoxic proteins into the B-cells [5].

Mosunetuzumab is the active pharmaceutical ingredient used in the Roche product Lunsumio [5].

A Manometric Respirometry Test according to OECD guideline no. 301 F showed that formulated Mosunetuzumab (including excipients) is readily biodegradable [1]. Additionally, as supporting information, acute ecotoxicity limit tests with green algae [2] and daphnids [3] consistently showed no significant adverse effects at the only tested concentration of 100 mg/L nominal concentration relating to the active substance Mosunetuzumab.

Considering human metabolism, rapid biodegradability and acute ecotoxicological properties of Mosunetuzumab, no exposure levels of concern to the environment are to be expected. This confirms the general finding that monoclonal antibodies and other protein or peptide active pharmaceutical substances are not expected to pose any risk to the environment [6].

Aquatic Toxicity Data for Mosunetuzumab

Study	Guideline	Results	Ref.
Algal growth inhibition test with *Raphidocelis subcapitata*	OECD 201	72 h EC50 (growth rate) >100 mg/L NC 72 h EC50 (yield) <100 mg/L NC [1)] 72 h NOEC <100 mg/L [1)]	[2]
Acute immobilisation test with *Daphnia magna*	OECD 202	48 h EC50 >100 mg/L NC 48 h NOEC 100 mg/L NC	[3]

EC50 concentration of the test substance that results in 50% effect
NC Nominal concentration
NOEC No Observed Effect Concentration
1) Artefact due to precipitation of the protein in the solution

Environmental Fate Data for Mosunetuzumab

Study	Guideline	Results	Ref.
Ready biodegradability test	OECD 301 F	BOD/ThOD (mineralisation) 97% after 28 days 89% at the end of the 10-day window Readily biodegradable DOC elimination 96% after 28 days	[1]

BOD Biochemical oxygen demand
DOC Dissolved organic carbon
ThOD Theoretical oxygen demand

References

[1] Arcadis Schweiz Ltd, on behalf of Genentech, Inc., South San Francisco, CA 94080 (2021): Mosunetuzumab – Ready biodegradability in an aqueous medium: manometric respirometry test. ACH study no. A20-01701

[2] Arcadis Schweiz Ltd, on behalf of Genentech, Inc., South San Francisco, CA 94080 (2021): Mosunetuzumab – Fresh water algal growth inhibition test with *Raphidocelis subcapitata*. ACH study no. A20-01699

[3] Arcadis Schweiz Ltd, on behalf of Genentech, Inc., South San Francisco, CA 94080 (2021): Mosunetuzumab – Acute immobilisation test with *Daphnia magna*. ACH study no. A20-01700

[4] European Medicines Agency (EMA) (2006/2015): Guideline on the environmental risk assessment of medicinal products for human use. European Medicines Agency, Committee for Medicinal Products for Human Use (CHMP), 01 June 2006, EMA/CHMP/SWP/447/00 corr 2

[5] F. Hoffmann-La Roche Ltd (2022): Media & Investor Release. European Commission approves Roche's first-in-class bispecific antibody Lunsumio for people with relapsed or refractory follicular lymphoma, 8 June 2022. https://www.roche.com/media/releases/med-cor-2022-06-08

[6] Straub JO (2010): Protein and Peptide Therapeuticals: An Example of "Benign by Nature" Active Pharmaceutical Ingredients. *In* Kümmerer K, Hempel M, eds: Green and Sustainable Pharmacy. Springer, Heidelberg, pp 127–133