Environmental Risk Assessment Summary
Satralizumab

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

Satralizumab is a humanised monoclonal antibody and the only approved therapy designed to target and inhibit interleukin-6 (IL-6) receptor activity, believed to play a key role in the inflammation associated with neuromyelitis optica spectrum disorder (NMOSD). The treatment was designed by Chugai, a member of the Roche group, using novel recycling antibody technology, which compared to conventional technology, allows for longer duration of antibody circulation and subcutaneous dosing every four weeks [6]. Satralizumab is the active pharmaceutical ingredient used in the Roche product Enspryng [5]. Enspryng is approved in Canada, Japan and Switzerland, as a monotherapy or in combination with baseline immunosuppressant therapy, for the treatment of NMOSD in adult and adolescent patients who are aquaporin-4 antibody (AQP4-IgG) seropositive. In the U.S., it is approved for adults living with anti-aquaporin-4 (AQP4) antibody-positive NMOSD (Roche Product Information).

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

Considering human metabolism, rapid biodegradability and acute ecotoxicological properties of Satralizumab, 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 [7].

Aquatic Toxicity Data for Satralizumab

Study	Guideline	Results	Ref.
Algal growth inhibition test with *Desmodesmus subspicatus*	OECD 201	72 h EC50 (growth rate) >100 mg/L NC 72 h EC50 (yield) >100 mg/L NC 72 h NOEC 100 mg/L NC	[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
LC50 concentration of the test substance that results in 50% mortality
NC Nominal concentration
NOEC No Observed Effect Concentration

Environmental Fate Data for Satralizumab

Study	Guideline	Results	Ref.
Ready biodegradability test	OECD 301 F	BOD/ThOD (mineralisation) 78% after 28 days 76% at the end of the 10-d window Readily biodegradable DOC elimination 98% after 28 days	[1]

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

References

[1] Arcadis Schweiz LTD, on behalf of F. Hoffmann-La Roche Ltd, Basel, Switzerland (2019): Satralizumab. Ready biodegradability – evaluation of the aerobic biodegradability in an aqueous medium: manometric respirometry test. Study no. A18-01681

[2] Arcadis Schweiz LTD, on behalf of F. Hoffmann-La Roche Ltd, Basel, Switzerland (2019): Satralizumab. Fresh water algal growth inhibition test with *Desmodesmus subspicatus*. Study no. A18-01679

[3] Arcadis Schweiz LTD, on behalf of F. Hoffmann-La Roche Ltd, Basel, Switzerland (2019): Satralizumab. 48-Hour acute toxicity to *Daphnia magna*. Study no. A18-01680

[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 (2020): Safety data sheet for Enspryng, 19 June 2020. https://www.roche.com/sustainability/environment/global_product_strategy_and_safety_data_sheets.htm

[6] F. Hoffmann-La Roche Ltd (2020): Media Release, 17 August 2020. https://www.roche.com/media/releases/med-cor-2020-08-17.htm

[7] 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