Summary of Risk Management Plan (RMP)

Radicava®

Solution for infusion

Edaravone 30 mg/100ml

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Based on RMP version 3.0

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Disclaimer

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of Radicava® is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation / Information sur le médicament" approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Radicava® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. Mitsubishi Tanabe Pharma GmbH, Düsseldorf, Zweigniederlassung Zürich, is fully responsible for the accuracy and correctness of the content of the published summary RMP of Radicava®.

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Summary of risk management plan for Radicava® (Edaravone)

This is a summary of the risk management plan (RMP) for Radicava®. The RMP details important risks of Radicava®, how these risks can be minimised, and how more information will be obtained about Radicava®'s risks and uncertainties (missing information).

Radicava®'s summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Radicava® should be used.

Important new concerns or changes to the current ones will be included in updates of Radicava®'s RMP.

I. The medicine and what it is used for

Radicava® is authorised for the treatment of patients with amyotrophic lateral sclerosis (ALS) (see SmPC for the full indication). It contains edaravone as the active substance and it is given by intravenous infusion.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Radicava®, together with measures to minimise such risks and the proposed studies for learning more about Radicava®'s risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size - the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status - the way a medicine is supplied to the patient (e.g. with prescription) - can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Radicava® is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Radicava® are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Radicava®. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information

Important identified risks	None
Important potential risks	• Hypersensitivity reaction, anaphylactic reaction
Missing information	• Patients with ALS severity grade > 3 and/or decreased respiratory function (%FVC <80%) • Long term safety (>12 cycles)

II.B Summary of important risks

The safety information in the approved Product Information is aligned to the reference medicinal product.

Additional pharmacovigilance activities are provided below for each missing information.

Important potential risk Hypersensitivity reaction, anaphylactic reaction	
Evidence for linking the risk to the medicine	Clinical study data, post-marketing data, literature
Risk factors and risk groups	Patients with ALS with history of hypersensitivity to edaravone or any of the inactive ingredients of edaravone.
Risk minimisation measures	Routine risk minimisation measures - SmPC section Contraindication - SmPC section Warnings and Preacautions Additional risk minimisation measures - No risk minimisation measures

Important Missing information Patients with ALS severity grade >3 and/or decreased respiratory function (%FVC <80%)	
Risk minimisation measures	Routine risk minimisation measures - No risk minimisation measures Additional risk minimisation measures - No risk minimisation measures

Important Missing information Long term safety (>12 cycles)	
Risk minimisation measures	Routine risk minimisation measures - No risk minimisation measures Additional risk minimisation measures - No risk minimisation measures

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Radicava®.

II.C.2 Other studies in post-authorisation development plan

Carcinogenicity studies:

Study short name

3208-1 A carcinogenicity study of edaravone, administered by a clinically relevant route, in mouse.

Purpose of the study: Required per U.S. FDA Health Authority as a condition for marketing authorization. Study is planned and design under development.

3208-2	A two-year carcinogenicity study of edaravone, administered by a clinically relevant route, in rat. Purpose of the study: Required per U.S. FDA Health Authority as a condition for marketing authorization. Study is planned and design under development.

Postmarketing studies:

Study short name	
MT-1186-A02	A randomized, double-blind, controlled trial of edaravone in patients with ALS (definite or probable, according to ALS El Escorial Revised Airlie House criteria). Purpose of the study: Required per U.S. FDA Health Authority as a condition for marketing authorization. The primary efficacy endpoint will be the change in the revised ALS functional rating scale score (ALSFRS-R) from baseline to the end of the study. The study duration will be at least 24 weeks.