Part VI: Summary of the risk management plan

Summary of risk management plan for Gadoteric Acid EXDRA (Gadoteric acid)

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

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

Important new concerns or changes to the current ones will be included in updates of Gadoteric Acid EXDRA's RMP.

I. The medicine and what it is used for

Gadoteric Acid EXDRA is authorised for:

Enhancement of the contrast in Magnetic Resonance Imaging (MRI) for a better visualization/delineation in:

Adult and paediatric population (0-18 years)

- MRI of the CNS including lesions of the brain, spine, and surrounding tissues
- Whole body MRI including lesions of the liver, kidneys, pancreas, pelvis, lungs, heart, breast, and musculoskeletal system.

Adult population

- MR angiography including lesions or stenoses of the non-coronary arteries.

(see SmPC for the full indication).

It contains gadoteric acid as the active substance and it is given by intravenous route only.

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

Important risks of Gadoteric Acid EXDRA, together with measures to minimise such risks and the proposed studies for learning more about Gadoteric Acid EXDRA'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 package leaflet and 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 or without prescription) can help to minimise its risks.

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

In the case of Gadoteric Acid EXDRA, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

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 Gadoteric Acid EXDRA is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Gadoteric Acid EXDRA 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 Gadoteric Acid EXDRA. 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	• Nephrogenic systemic fibrosis (NSF)
Important potential risks	• Adverse clinical effects of accumulation and retention of gadolinium in organs and tissues other than brain tissues • Adverse clinical effects of accumulation and retention of gadolinium in the brain
Missing information	• Clinical significance of gadolinium accumulation in organs and tissues other than brain tissues • Clinical significance of gadolinium retention in the brain • Safety in pregnancy and lactation

II.B Summary of important risks

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

Important identified risk: Nephrogenic systemic fibrosis	
Risk minimisation measures	Routine risk minimisation measures: This risk is adequately addressed through appropriate wording in the SmPC and PIL for Gadoteric Acid EXDRA as mentioned in the sections below: • SmPC sections 4.2, 4.4, 4.6, 4.8 and 4.9. • PIL section 2, 4. Traceability of the product administered: Gadoteric Acid EXDRA label (on vials) have a peel-off tracking label (with the name of the product and batch number) which can be stuck onto the patient's file. This is described in: • SmPC section 6.6. • PIL section 6. Other routine risk minimisation measures beyond the Product Information: Legal status: Medicinal product subject to medical prescription. Additional risk minimisation measures: None.

Important potential risk: Adverse clinical effects of accumulation and retention of gadolinium in organs and tissues other than brain tissues	
Risk minimisation measures	Routine risk minimisation measures: This risk is adequately addressed through an appropriate wording in the SmPC for Gadoteric Acid EXDRA as mentioned below: • SmPC sections 4.1 and 4.2. Other routine risk minimisation measures beyond the Product Information: Legal status: Medicinal product subject to medical prescription. Additional risk minimisation measures:

Important potential risk: Adverse clinical effects of accumulation and retention of gadolinium in organs and tissues other than brain tissues	
	None.

Important potential risk: Adverse clinical effects of accumulation and retention of gadolinium in the brain	
Risk minimisation measures	Routine risk minimisation measures: This risk is adequately addressed through appropriate wording in the sections of the SmPC and PIL as follows: • SmPC sections 4.1 and 4.2. Other routine risk minimisation measures beyond the Product Information: Legal status: Medicinal product subject to medical prescription. Additional risk minimisation measures: None.

Missing information: Clinical significance of gadolinium accumulation in organs and tissues other than brain tissues.	
Risk minimisation measures	Routine risk minimisation measure: This risk is adequately addressed through appropriate wording in the sections of the SmPC and PIL as follows: • SmPC sections 4.1 and 4.2. Other routine risk minimisation measures beyond the Product Information: Legal status: Medicinal product subject to medical prescription. Additional risk minimisation measures: None.

Missing information: Clinical significance of gadolinium retention in the brain.	
Risk minimisation measures	Routine risk minimisation measures This risk is adequately addressed through appropriate wording in the sections of the SmPC and PIL as follows: • SmPC sections 4.1 and 4.2. Other routine risk minimisation measures beyond the Product Information: Legal status: Medicinal product subject to medical prescription. Additional risk minimisation measures: None.

Missing information: Safety in pregnancy and lactation.	
Risk minimisation measures	Routine risk minimisation measure: This risk is adequately addressed through appropriate wording in the sections of the SmPC and PIL as follows: • SmPC sections 4.6 and 5.3. • PIL section 2. Other routine risk minimisation measures beyond the Product Information: Legal status: Medicinal product subject to medical prescription. Additional risk minimisation measures: None.

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 Gadoteric Acid EXDRA.

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

There are no studies required for Gadoteric Acid EXDRA.