

Summary of the Risk Management Plan for Ambelvist

Active substance: Gadoquatrane

Version number: 1.0

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Based on the EU-RMP v0.2 for Ambelvist (dated 18-MAR-2026)



AMBELVIST®
(Gadoquatrane)
Risk Management Plan
Summary of activities in the risk management plan

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 Ambelvist 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 Ambelvist in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. Bayer (Schweiz) AG is fully responsible for the accuracy and correctness of the content of the published RMP summary of Ambelvist.

The Summary of Risk Management Plan for Ambelvist (Gadoquatrane) v1.0 is based on the Summary of the Risk Management Plan for Ambelvist (Gadoquatrane) of the EU-RMP v0.2, dated 18-MAR-2026.

Summary of activities in the risk management plan

Summary of risk management plan for Ambelvist (gadoquatrane)

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

Ambelvist product information, a document describing the properties and the officially approved conditions of use, give essential information to healthcare professionals and patients on how Ambelvist should be used.

Important new concerns or changes to the current ones will be included in updates of the Ambelvist RMP.

I. The medicine and what it is used for

Ambelvist is for diagnostic use only. Ambelvist is indicated for contrast enhancement in magnetic resonance imaging (MRI) to detect and visualize known or suspected pathology in the central nervous system (CNS) and body, in adult and paediatric patients of all ages¹.

It contains gadoquatrane as the active substance and it is given by intravenous injection.

Further information about the evaluation of gadoquatrane benefits can be found in Ambelvist EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

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

Important risks of Ambelvist, together with measures to minimise such risks and the proposed studies for learning more about Ambelvist 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 as 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.

¹ In Switzerland, Ambelvist is authorised for use in adult and paediatric patients aged 12 years and older only.

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

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

II.A List of important risks and missing information

Important risks of Ambelvist 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 an association with the use of Ambelvist. 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).

Table 1: Summary of safety concerns

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 the brain • Adverse clinical effects of accumulation and retention of gadolinium in organs and tissues other than brain tissues
Missing information	• Clinical significance of gadolinium retention in the brain • Clinical significance of gadolinium accumulation in organs and tissues other than brain tissues • Safety of use in pregnancy and lactation

II.B Summary of important risks

Table 2: Important identified risk: Nephrogenic systemic fibrosis (NSF)

Evidence for linking the risk to the medicine	Nephrogenic systemic fibrosis is a rare fibrosing disorder of possible multi-factorial etiology that occurs exclusively in patients with severe renal impairment after receiving GBCAs. It is an identified or potential risk for all GBCAs based on non-clinical studies, published literature and post-marketing experience. The cumulative data from all sources suggest that the risk of developing NSF after receiving macrocyclic GBCAs such as Ambelvist is very low.
Risk factors and risk groups	Patients with acute or chronic severe renal impairment (eGFR <30 mL/min/1.73 m ²), acute renal insufficiency of any severity due to hepato-renal syndrome, and patients in the peri-operative liver transplantation period receiving GBCAs are assumed to be at increased risk for NSF. High and/or repeated doses of GBCAs in these at-risk populations have been suggested to be a possible risk

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Table 2: Important identified risk: Nephrogenic systemic fibrosis (NSF)

	factor for development of NSF. Regulatory authorities including FDA and EMA have classified the marketed GBCAs into risk groups based on the complex stability of the gadolinium-chelates. Macrocyclic agents (such as Ambelvist) are in the lowest risk class. Furthermore, the clinical dose of Ambelvist is relevantly reduced compared to available standard dose of the SoC GBCAs.
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.2, 4.4 and 4.8 (Description of selected adverse reactions) • SmPC section 6.6 (peel-off tracking label) • Prescription-only medicine, administered by health care professionals, for diagnostic purposes. Additional risk minimisation measures: • None

Abbreviations: eGFR: Estimated glomerular filtration rate; EMA: European Medicines Agency; FDA: Food and Drugs Administration; GBCA: Gadolinium-based contrast agent; MRI: Magnetic resonance imaging; NSF: Nephrogenic systemic fibrosis; SmPC: Summary of Product Characteristics; SoC: Standard of Care.

Table 3: Important potential risk: Adverse clinical effects of accumulation and retention of gadolinium in the brain

Evidence for linking the risk to the medicine	Non-clinical and clinical studies with GBCAs have shown that small amounts of gadolinium may be detectable in the brain, especially after multiple, high dose or closely spaced CE-MRI procedures, and with greater retention at equivalent doses in multi-purpose linear agents. Gadolinium has been measured in the brain on autopsy and necropsy in both humans and animals. To date, no adverse health effects have been confirmed to be related to this finding. Evidence suggests that less gadolinium may be present in the brain with Ambelvist, because of its lower dose compared to other SoC GBCAs at standard dose.
Risk factors and risk groups	No risk factors other than frequent, repeated use of GBCAs have been identified. Patients who receive repeated and/or high dose contrast-enhanced MRIs may be most at risk. It may be assumed that patients with CNS diseases/a disrupted blood-brain barrier might be at an increased risk for entry of GBCA/Gd into the brain, as that is the mechanism by which the efficacy of GBCAs in CNS indications is achieved. Patients with renal insufficiency have a delayed excretion of GBCAs and therefore may be at increased risk for a longer period of exposure; however, the increased signal intensity has been observed in patients with and without renal impairment. Because of Ambelvist low dose (60% reduced Gd dose compared to other SoC GBCAs at the standard dose), it is less likely to result in presence of gadolinium than other multi-purpose SoC GBCAs at standard dose (0.1 mmol/kg bw).

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Table 3: Important potential risk: Adverse clinical effects of accumulation and retention of gadolinium in the brain

Risk minimisation measures	Routine risk minimisation measures: • SmPC section 6.6 (peel-off tracking label) • Prescription-only medicine, administered by health care professionals, for diagnostic purposes. Additional risk minimisation measures: • None
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Abbreviations: bw: body weight; CE-MRI: Contrast-enhanced magnetic resonance imaging; CNS: Central nervous system; GBCA: Gadolinium-based contrast agent; Gd: Gadolinium; MRI: Magnetic resonance imaging; SoC: Standard of care.

Table 4: Important potential risk: Adverse clinical effects of accumulation and retention of gadolinium in organs and tissues other than brain tissues

Evidence for linking the risk to the medicine	There have been reports of unexpectedly prolonged presence of gadolinium in organs and tissues other than the brain (for example, in bones) after repeated use of GBCAs. No risk factors other than frequent, repeated use of GBCAs have been identified. Gadolinium has been definitively measured in various organs by scientific methods including ICP-MS; however, it has not been confirmed that any adverse health effects are related to gadolinium presence in patients with normal renal function. Reports of persistent symptoms and elevated gadolinium levels in laboratory tests have been received concerning patients with normal renal function who received GBCAs. A causal relationship has not been established.
Risk factors and risk groups	Patients with severe renal impairment (eGFR <30 mL/min/1.73 m ²) or acute kidney injury are considered to be at increased risk for NSF (which may be associated with the presence of gadolinium in the skin or other organs). Patients who receive high and/or repeated dosing of GBCAs, especially when closely spaced, would be considered to be at higher risk for presence of higher concentrations of gadolinium in the body. Because of Ambelvist lower dose compared to SoC GBCAs at standard dose, it is less likely to result in prolonged presence of gadolinium than other multi-purpose GBCAs at standard dose. No adverse health effects from gadolinium retention have been confirmed in patients with normal renal function.

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Table 4: 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: • SmPC sections 4.2, 4.4 and 4.8 (Description of selected adverse reactions) • SmPC section 6.6 (peel-off tracking label) • Prescription-only medicine, administered by health care professionals, for diagnostic purposes. Additional risk minimisation measures: • None
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Abbreviations: eGFR: Estimated glomerular filtration rate; GBCA: Gadolinium-based contrast agent; ICP-MS: Inductively coupled plasma mass spectrometry; SmPC: Summary of Product Characteristics.

Table 5: Missing information: Clinical significance of gadolinium retention in the brain

Risk minimisation measures	Routine risk minimisation measures: • SmPC section 6.6 (peel-off tracking label) • Prescription-only medicine, administered by health care professionals, for diagnostic purposes. Additional risk minimisation measures: • None
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Table 6: Missing information: Clinical significance of gadolinium accumulation in organs and tissues other than brain tissues

Risk minimisation measures	Routine risk minimisation measures: • SmPC sections 4.2, 4.4 and 4.8 (description of selected adverse reactions) • SmPC section 6.6 (peel-off tracking label) • Prescription-only medicine, administered by health care professionals, for diagnostic purposes. Additional risk minimisation measures: • None
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Abbreviations: SmPC: Summary of Product Characteristics.

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Table 7: Missing information: Safety of use in pregnancy and lactation

Risk minimisation measures	Routine risk minimisation measures: • SmPC Section 4.6 mentions that Ambelvist should not be used during pregnancy unless the clinical condition of the woman requires its use. • SmPC Section 4.6 mentions that continuing or discontinuing breastfeeding for a period of 24 hours after administration of Ambelvist should be at discretion of the doctor and breastfeeding mother. • Prescription-only medicine, administered by health care professionals, for diagnostic purposes. Additional risk minimisation measures: • None
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Abbreviations. SmPC: Summary of Product Characteristics.

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 Ambelvist.

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

There are no studies required for Ambelvist.