## VI.2 Elements for a public summary

### *VI.2.1 Overview of disease epidemiology*

Gadoteric acid Sanochemia is used as a diagnostic agent for Magnetic Resonance Imaging (MRI) scans and improves the visualisation and delineation of:

- defects (lesions) in brain, spinal cord and adjacent tissue;
- defects (lesions) in liver, kidneys, pancreas, pelvis, lungs, heart, breast and musculoskeletal system;
- defects (lesions) and narrowing (stenosis) in arteries, except in coronary arteries.

### *VI.2.2 Summary of treatment benefits*

As Gadoteric acid Sanochemia is no treatment but only used for diagnostic purposes, the usage of Gadoteric acid Sanochemia is not associated with a particular disease. Therefore this section is not applicable for Gadoteric acid Sanochemia.

### *VI.2.3 Unknowns relating to treatment benefits*

As Gadoteric acid Sanochemia is no treatment but only used for diagnostic purposes, the summary of treatment benefits is not applicable.

### *VI.2.4 Summary of safety concerns*

***Important identified risks***

| Risk | What is known | Preventability |
|---|---|---|
| Risk of nephrogenic systemic fibrosis | In patients who suffer from severe kidney problems, or who are about to have or had recently had a liver transplant, the use of gadolinium-containing contrast agents has been associated with a disease called nephrogenic systemic fibrosis (NSF).<br>Isolated cases of nephrogenic systemic fibrosis (NSF) have been reported with the acive ingredient of Gadoteric acid Sanochemia (gadoteric acid), most of which were in patients co-administered other gadolinium-containing contrast agents. NSF is a disease involving thickening of the skin and connective tissues. NSF may result in severe joint immobility, muscle weakness or may affect the normal working of internal organs which may potentially be life threatening. | Prior to administration of Gadoteric acid Sanochemia, it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests.<br><br>As there is a possibility that NSF may occur with Gadoteric acid Sanochemia, it should therefore only be used in patients who suffer from severe kidney problems (GFR < 30 ml/min/1.73m2) and in patients who have recently had, or soon expect to have, a liver transplant, after careful risk/benefit assessment and if the diagnostic information is essential and not available without contrast-enhanced investigations.<br><br>As the kidney function of newborn babies and infants is not fully |

| Risk | What is known | Preventability |
|---|---|---|
| | | developed, Gadoteric acid Sanochemia should also only be given to new-born babies and infants up to one year of age.after careful consideration. |
| Risk of hypersensitivity reactions | There is a small risk that patients may have an allergic reaction to gadoteric acid. The frequency of this risk is uncommon and may affect up to 1 in 100 people. Such reactions can be severe and result in shock. The following symptoms may be the first signs of a shock. The doctor, radiologist or health care professional should be immediately informed if any of them are felt:<br>• swelling of the face, mouth or throat which may cause difficulties in swallowing or breathing<br>• swelling of hands or feet<br>• lightheadedness (hypotension)<br>• breathing difficulties<br>• whistling respiration<br>• coughing<br>• itching<br>• runny nose<br>• sneezing<br>• eye irritation<br>• hives<br>• skin rash | If there is a known allergy (hypersensitivity) to gadoteric acid or any of the other ingredients of Gadoteric acid Sanochemia, it should not be used.<br><br>If an allergic reaction occurs, the radiologist/doctor will stop the administration of the contrast medium at once and, if necessary, will start appropriate treatment of the allergic reactions. |

***Important potential risks***

| Risk | What is known |
|---|---|
| Teratogenicity | There are no data from the use of Gadoteric acid Sanochemia in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to use during pregnancy. Gadoteric acid Sanochemia should not be used during pregnancy unless the clinical condition of the woman requires use of gadoteric acid. |
| Convulsions | Like with other gadolinium containing contrast agents special precaution is necessary in patients with a low threshold for convulsions or who are being treated for epilepsy.<br>Precautionary measures should be taken by the physician, e.g. close monitoring. All equipment and drugs necessary to counter any convulsions which may occur must be made ready for use beforehand. |

**Missing information**

| Risk | What is known |
|---|---|
| Accumulation of gadolinium in bones, including long-term effects. | There is limited information on the accumulation of gadolinium in the bones. For this reason studies are planned/on-going to further investigate this issue. |

### *VI.2.5 Summary of additional risk minimisation measures by safety concern*

These additional risk minimisation measures are for the following risks:

**Risk of Nephrogenic Systemic Fibrosis**

| **Risk minimisation measure:** Detachable (“sticky” labels) |
|---|
| **Objective and rationale** |
| Detachable (“sticky”) labels on the vials of the Gadolinium-containing products, in order to have a harmonised traceability method across Europe for the effective monitoring of the use of Gadolinium-containing products and to enable reliable identification of Gadolinium –containing contrast agents to compare the risk between various Gadolinium –containing contrast agents. |
| **Risk minimisation measure:**<br>Education of prescribers and physicians who manage renally impaired patients. |
| **Objective and rationale** |
| Education of prescribers and physicians who manage patients with kidney problems..<br>To inform and educate the prescribers i.e. physicians to:<br>o Use Gadolinium – containing contrast agents only after careful evaluation of the need for patients with severe kidney problems<br>o Use of the smallest amount of gadolinium as necessary for a reliable diagnosis.<br>o Be informed how to suspect and confirm a diagnosis of nephrogenic systemic fibrosis (NSF).<br>o Be informed how to report any NSF case to the local Health Authorities, and/or Sanochemia if Gadoteric acid Sanochemia is used. |

### *VI.2.6 Planned post authorisation development plan (if applicable)*

**List of studies in post authorisation development plan**

Not applicable

**Studies which are a condition of the marketing authorisation (if applicable)**

The study mentioned in the table above is a condition of the marketing authorisation of the originator product Dotarem®.

### *VI.2.7 Summary of changes to the risk management plan over time*

**Table 2.** Major changes to the Risk Management Plan over time

| Version | Date | Safety Concerns | Comment |
|---|---|---|---|
| 1 | Sign off date: 29.11.2013 | Identified Risks:<br>• Nephrogenic Systemic Fibrosis<br>• Hypersensitivity reactions<br><br>Missing information:<br>• Long-term accumulation of gadolinium in bone<br>• Pregnancy data | First version |
| 1.1 | Sign off date: 31.08.2014 | Important identified Risks:<br>• Nephrogenic Systemic Fibrosis<br>• Hypersensitivity reactions<br><br>Important potential risks:<br>• Teratogenicity<br>• Convulsions<br>Missing information:<br>• Long-term accumulation of gadolinium in bone<br>• Pregnancy data | Updated during marketing authorisation procedure, according to RMS day 70 preliminary assessment report |
| 1.2 | Sign off date: 23.03.2015 | Important identified Risks:<br>• Nephrogenic Systemic Fibrosis<br>• Hypersensitivity reactions<br><br>Important potential risks:<br>• Teratogenicity<br>• Convulsions<br>Missing information:<br>• Long-term accumulation of gadolinium in bone<br>• Pregnancy data | No changes in Safety Concerns; RMP was updated during marketing authorisation procedure, according to RMS day 120 draft assessment report |