Annex I

Scientific conclusions and grounds for the variation to the terms of the Marketing Authorisation(s)

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for gadoteric acid (IV and intravascular formulations), the scientific conclusions are as follows:

In view of available data on administration during pregnancy; and intrathecal administration from the literature, spontaneous reports and in view of a plausible mechanism of action, the PRAC considers a causal relationship between gadoteric acid and risks due to use during pregnancy and intrathecal administration. The PRAC concluded that the product information of products containing gadoteric acid should be amended accordingly.

The CMDh agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the Marketing Authorisation(s)

On the basis of the scientific conclusions for gadoteric acid (IV and intravascular formulations) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing gadoteric acid (IV and intravascular formulations) is unchanged subject to the proposed changes to the product information.

The CMDh reaches the position that the marketing authorisation(s) of products in the scope of this single PSUR assessment should be varied. To the extent that additional medicinal products containing gadoteric acid (IV and intravascular formulations) are currently authorised in the EU or are subject to future authorisation procedures in the EU, the CMDh recommends that the concerned Member States and applicant/marketing authorisation holders take due consideration of this CMDh position.

Annex II

Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Product Information (new text **underlined and in bold**, deleted text ~~strike through~~)

Summary of Product Characteristics

- Section 4.4

~~Do not use by intrathecal route.~~ **Gadoteric acid must not be used intrathecally. Serious, life-threatening and fatal cases, primarily with neurological reactions (e.g. coma, encephalopathy, seizures), have been reported with intrathecal use.** Gadoteric acid should be strictly administered via intravenous injection**. E**xtravasation may result in local intolerance reactions, requiring the usual local care"

- Section 4.6

New information on the risk(s) of the product when used during pregnancy should be added as follows:

Pregnancy

~~There are no data~~ **Data** on the use of **gadolinium-based contrast agents including** gadoteric acid in pregnant women **is limited. Gadolinium can cross the placenta. It is unknown whether exposure to gadolinium is associated with adverse effects in the foetus.** Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). Gadoteric acid should not be used during pregnancy unless the clinical condition of the woman requires use of gadoteric acid.

Package Leaflet

- Section 2 – Pregnancy and breast-feeding

Pregnancy
Gadoteric acid can cross the placenta. It is not known whether it affects the baby. Xxx should not be used during pregnancy unless strictly necessary.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	08 March 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	09 May 2024