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 gadoteridol, 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 gadoteridol and risks due to use during pregnancy and intrathecal administration is at least a reasonable possibility. The PRAC concluded that the product information of products containing gadoteridol should be amended accordingly.

Having reviewed the PRAC recommendation, the CMDh agrees with the PRAC overall conclusions and grounds for recommendation.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for gadoteridol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing gadoteridol is unchanged subject to the proposed changes to the product information.
The CMDh recommends that the terms of the marketing authorisation(s) should be varied.

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

A warning should be added as follows:

[…]
In patients suffering from epilepsy or brain lesions the likelihood of convulsions during the examination may be increased. Precautions are necessary when examining these patients (e.g. monitoring of the patient) and the equipment and medicinal products needed for the rapid treatment of possible convulsions should be available.

Gadoteridol 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.

- 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 from~~ **Data on** the use of **gadolinium-based contrast agents including** gadoteridol 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). ProHance should not be used during pregnancy unless the clinical condition of the woman requires use of gadoteridol.

Package Leaflet

- Section 2 – Pregnancy and breast-feeding

Pregnancy

Gadoteridol can cross the placenta. It is not known whether it affects the baby. You must tell your doctor if you think you are or might become pregnant […]

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