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 gadobutrol, 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 gadobutrol 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 gadobutrol 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 gadobutrol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing gadobutrol 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:

Gadobutrol 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 with regards to 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** gadobutrol 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.** [...|

Package Leaflet

- Section 2 – Pregnancy and breast-feeding

Pregnancy

Gadobutrol 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:	10 March 2024
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	09 May 2024