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 iobitridol, the scientific conclusions are as follows:

In view of available data on contrast encephalopathy from the literature and spontaneous reports including in some cases a close temporal relationship, and in view of a plausible mechanism of action, the PRAC considers a causal relationship between iobitridol and contrast encephalopathy is at least a reasonable possibility. The PRAC concluded that the product information of products containing iobitridol 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 iobitridol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing iobitridol 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:

4.4.2 Precautions for use

…

4.4.2.x. Central nervous system disorders

Encephalopathy has been reported with the use of iobitridol (see section 4.8). Contrast-induced encephalopathy may manifest with symptoms and signs of neurological dysfunction such as headache, visual disturbance, cortical blindness, confusion, seizures, loss of coordination, hemiparesis, aphasia, unconsciousness, coma, and cerebral oedema. Symptoms usually occur within minutes to hours after administration of iobitridol and generally resolve within days.

Factors which increase blood-brain barrier permeability facilitate the passage of the contrast medium into cerebral tissue, which can lead to central nervous system reactions, e.g. encephalopathy. If contrast encephalopathy is suspected, appropriate medical management should be initiated and iobitridol should not be readministered.

…

- Section 4.8

The following adverse reaction should be added under the SOC Nervous systems disorders with a frequency of 'unknown':

Contrast encephalopathy*

***Contrast encephalopathy may manifest with symptoms and signs described in section 4.4**

Package Leaflet

Section 2

Warnings and precaution

Special precautions with [product name]

[...]

During or shortly after the imaging procedure you may experience a short-term brain disorder called encephalopathy. Seek medical attention immediately if you notice any of the symptoms related to this condition described in section 4.

Section 4

[...]

Not Known: based on available data the frequency cannot be defined.

Short term brain disorders (encephalopathy) which can cause headache, confusion, difficulties with vision, loss of vision, seizures, loss of coordination, weakness on one side of the body, problems with speech and loss of consciousness.

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	January 2025 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	16 March 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	15 May 2025