

EN

## **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 iodixanol, the scientific conclusions are as follows:

In view of available data on risks from the literature and spontaneous reports, the Lead Member State considers that product information of products containing iodixanol should be amended to further describe the risk of encephalopathy and to provide risk minimisation recommendations.

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 iodixanol the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing iodixanol 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 iodixanol 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**

**Encephalopathy has been reported with the use of iodixanol (see section 4.8). Contrast 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 within minutes to hours after administration of iodixanol, and generally resolves within days.**

**The product should be used with caution in patients with conditions that disrupt the integrity of the blood brain barrier (BBB), potentially leading to increased permeability of contrast media across the BBB and increasing the risk of encephalopathy.** Patients with acute cerebral pathology, tumours or a history of epilepsy are predisposed for seizures and merit particular care. Also, alcoholics and drug addicts have an increased risk for seizures and neurological reactions. In regard to intravascular application care should be taken in patients with acute stroke or acute intracranial bleeding, in patients with altered blood brain barrier, cerebral oedema or acute demyelination.

**If contrast encephalopathy is suspected, administration of iodixanol should be discontinued and appropriate medical management should be initiated.**

## Package leaflet

- **Section 2**

**During or shortly after the imaging procedure you may experience a short-term brain disorder called encephalopathy. Tell your doctor straight away if you notice any of the symptoms related to this condition described in Section 4.**

- **Section 4**

Short term brain disorders (encephalopathy) which can cause confusion, memory loss, hallucinations, ~~and movement problems,~~ **difficulties with vision, loss of vision, seizures, loss of coordination, loss of movement in 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 2021 CMDh meeting |
| Transmission to National Competent Authorities of the translations of the annexes to the position:                       | 14 March 2021             |
| Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder): | 13 May 2021               |