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 daunorubicin, the scientific conclusions are as follows:

Based on the review of relevant case reports, the results of the close monitoring and the review of scientific literature, the PRAC considers that inclusion of a warning on Posterior Reversible Encephalopathy Syndrome (PRES) with the administration of daunorubicin-containing combination chemotherapy in the section 4.4 of the Summary of Product Characteristics is warranted; in addition, the adverse reaction “infections” should be amended with a footnote below the table of adverse reactions with the information that these infections can result in a fatal outcome.

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

Posterior reversible encephalopathy syndrome (PRES):

Cases of PRES have been reported with daunorubicin used in combination chemotherapy. PRES is a neurological disorder which can present with headache, seizure, lethargy, confusion, blindness and other visual and neurologic disturbances. Mild to severe hypertension may be present. Magnetic resonance imaging is necessary to confirm the diagnosis of PRES. In patients with PRES, the discontinuation of daunorubicin treatment should be considered.

Section 4.8

The adverse reaction "Infections" already included in the table of adverse reactions should be amended as follow: "Infections"*** […] *which sometimes can be fatal**, as footnote below the table of adverse reactions.

Package Leaflet

- Take special care with daunorubicin

A neurological disorder called PRES has been reported when treatment with daunorubicin has been used in combination with other cancer treatments. PRES can cause symptoms such as headache, seizures, lethargy, confusion and disturbed vision. If you experience any of these symptoms you should contact your doctor

- Possible side effects

Infections, which sometimes can be fatal

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	February 2019 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	6 April 2019
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	5 June 2019