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 oxaliplatin, the scientific conclusions are as follows:

In view of available data on haemolytic anaemia with positive Coombs test from spontaneous cases and the literature, including in some cases confirmed oxaliplatin-IgG antibody complex using direct antiglobulin test (DAT), the PRAC considers a causal relationship between oxaliplatin and Coombs positive haemolytic anaemia is at least a reasonable possibility. The PRAC concluded that the product information of products containing oxaliplatin should be amended accordingly. This adverse drug reaction should be distinguished from microangiopathic haemolytic anaemia which occurs in the context of haemolytic uraemic syndrome.

In view of available data on splenomegaly from clinical cases and the literature which highlighted that splenomegaly is the clinical consequence of already known adverse drug reactions (sinusoidal obstruction syndrome/portal hypertension), the PRAC concluded that product information of products containing oxaliplatin should be amended to include splenomegaly in the current warning about liver disorders.

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 oxaliplatin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing oxaliplatin 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 amended as follows:

Liver disorders

In case of abnormal liver function test results, **splenomegaly** or portal hypertension which does not obviously result from liver metastases, very rare cases of drug-induced hepatic vascular disorders should be considered.

- Section 4.8:

The following footnote should be added:

MedDRA system organ classes	Frequency
Blood and lymphatic system disorders	Haemolytic anaemia*** [rare]

***Microangiopathic haemolytic anaemia associated with haemolytic uraemic syndrome (HUS) or Coombs positive haemolytic anaemia, see section 4.4)**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2024 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	26 January 2025
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	27 March 2025