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 hydroxycarbamide (except for centrally authorised product), the scientific conclusions are as follows:

In view of available data on hemolytic anemia from the literature and spontaneous reports and in view of a plausible mechanism of action, the PRAC considers a causal relationship between hydroxycarbamide (except for centrally authorised product) and haemolytic anaemia is established. The PRAC concluded that the product information of products containing hydroxycarbamide (except for centrally authorised product) should be amended accordingly.

Update of sections 4.4 and 4.8 of the SmPC to add a warning on occurrence of hemolytic anemia and the adverse reaction Hemolytic anemia with a frequency not known.

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 hydroxycarbamide (except for centrally authorised product) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing hydroxycarbamide (except for centrally authorised product) 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 hydroxycarbamide (except for centrally authorised product) 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

A warning should be added as follows:

Cases of hemolytic anemia in patients treated with hydroxycarbamide for myeloproliferative diseases have been reported. Patients who develop severe anemia should have laboratory tests evaluated for hemolysis. If diagnosis of hemolytic anemia is established, hydroxycarbamide should be discontinued.

- Section 4.8

The following adverse reaction should be added under the SOC Blood and lymphatic system disorders with a frequency not known:

Hemolytic anemia

Package Leaflet

2. What you need to know before you <take> <use> X

Warnings and precautions

Talk to your doctor <or> <pharmacist> <or nurse> before <taking> <using> X

If hemolytic anemia (disorder in which red blood cells are destroyed faster than they can be made) is detected when the blood tests are checked, your doctor will stop treatment with X.

4. Possible side effects

The following adverse reaction should be added:

Not known: frequency cannot be estimated from the available data

Hemolytic anemia

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	July 2021 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	5 September 2021
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	4 November 2021