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 rabbit anti-humanT-lymphocyte immunoglobulin, the scientific conclusions are as follows:

Regarding the adverse drug reaction “anaemia”, it is already listed in product information of some rabbit anti-humanT-lymphocyte immunoglobulin products. Furthermore, the myelosupressive effect is known for anti-thymocyte globulin and can be a causative factor of anaemia. Therefore PRAC recommends to add the adverse reaction “anaemia” in the section 4.8 of the Summary of Product Characteristics with a frequency “very common”.

Regarding the adverse reaction “hyperbilirubinemia”, it is a listed adverse drug reaction for Grafalon. Furthermore, based on the literature article and EudraVigilance Data Analysis System data there is sufficient evidence of causal relationship between Hyperbilirubinemia and rabbit anti-humanT-lymphocyte immunoglobulin. Therefore PRAC recommends to add the adverse reaction “hyperbilirubinemia” in the section 4.8 of the Summary of Product Characteristics with a frequency “unknown”.

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 rabbit anti-humanT-lymphocyte immunoglobulin the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing rabbit anti-humanT-lymphocyte immunoglobulin 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 rabbit anti-humanT-lymphocyte immunoglobulin 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**)

Summary of Product Characteristics

- Section 4.8

The following adverse reaction should be added under the SOC “Hepatobiliary disorders” with a frequency “unknown”:

Hyperbilirubinaemia

The following adverse reaction should be added under the SOC “Blood and lymphatic system disorders” with a frequency “very common”:

Anaemia

Package Leaflet

- Section 4

Frequency not known (frequency cannot be estimated from the available data)

Increased bilirubin in the blood (elevation of laboratory parameter)

Very common side-effects (may affect more than 1 in 10 people):

Low count of red blood cells (anaemia)

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

APPENDIX I

PRAC PSUR Assessment Report