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 glucosamine, the scientific conclusions are as follows:

Further to a review of concomitant uses of glucosamine with oral vitamin K antagonists, the PRAC concluded that the provided dataset supports evidence of interactions which may lead to an increase of the International Normalised Ratio (INR) after patients receiving coumarin anticoagulants began taking glucosamine, which indicates an increase in the coagulation time. Whilst acknowledging that there is insufficient information to conclude on a mechanism for an interaction between glucosamine and coumarin anticoagulants, the Committee notices the evidence of an interaction between glucosamine and coumarin anticoagulants by the observation that in the majority of cases the INR began to fall to normal values when glucosamine intake is discontinued. The Committee therefore agreed that amendments to the sections 4.5 of the SmPC are warranted for the glucosamine and oral vitamin K antagonists interaction. The Package leaflet is updated accordingly.

Therefore, in view of the data presented in the reviewed PSURs, the PRAC considered that changes to the product information of medicinal products containing glucosamine, were warranted.

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 glucosamine the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing glucosamine 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 glucosamine 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 4.5

The following statement should be added:

There are limited data on possible drug interactions with glucosamine, but increments in the INR parameter have been reported with oral vitamin K antagonists. Patients treated with oral vitamin K antagonists should therefore be closely monitored at the time of initiation or termination of glucosamine therapy.

Package Leaflet

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

Other medicines and X

Caution should be exercised if X have to be combined with other medicines, especially with:

- **Some types of medicines used to prevent blood clotting (e.g. warfarin, dicoumarol, phenprocoumon, acenocoumarol and fluidione). The effect of these medicines may be stronger when used with glucosamine. Patients treated with such combinations should therefore be monitored extra carefully when initiating or ending glucosamine therapy.**

Annex III

Timetable for the implementation of this position

Timetable for the implementation of this position

Adoption of CMDh position:	December 2017 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the position:	27 January 2018
Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder):	28 March 2018