# 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 interferon alpha-2a, the scientific conclusions are as follows:

In view of the reported cases of hearing impairment during the review period and also considering that there is a possible mechanism of action and that hearing impairment is already included in the product information of other interferon containing products, the PRAC considered that hearing impairment should be included as an adverse drug reaction (ADR) in section 4.8 of the summary of product characteristics (SmPC) of interferon alpha-2a with a frequency not known. Furthermore, based on reported cases of skin depigmentation, all the available evidence from literature, and also taking into account that there is a biological plausibility of interferon alpha-2a induced depigmentation, the PRAC considered that skin depigmentation should be added as an ADR in section 4.8 of the SmPC with a frequency not known. The package leaflet is updated accordingly.

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 interferon alpha-2a the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing interferon alpha-2a 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 interferon alpha-2a 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 4.8

*[The following adverse reaction should be added under the SOC Skin and subcutaneous tissue disorders with a frequency 'not known']*

**- skin depigmentation**

*[The following adverse reaction should be added under the SOC Ear and labyrinth disorders with a frequency 'not known']*

- **hearing impairment**

**Package Leaflet**

- Section 4: Possible side effects

*[The following adverse reaction should be added as follows]*

*Not known side effects:*

*[…]*
**Ear disorders: Hearing loss**
**Skin disorders: Discolouration of the skin**

## Annex III

## Timetable for the implementation of this position>

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|---|---|
| Adoption of CMDh position: | February, 2018 CMDh meeting |
| Transmission to National Competent Authorities of the translations of the annexes to the position: | 07 April 2018 |
| Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder): | 06 June 2018 |