# 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 irinotecan (except for liposomal formulations), the scientific conclusions are as follows:

Based on the cumulative review of cases reporting fungal, viral and opportunistic infections with irinotecan from clinical trials and post-marketing experience, a contributory role for irinotecan cannot be excluded, especially considering the myelosuppression associated with irinotecan and the resulting increase in susceptibility to infections. Therefore, the PRAC recommends an update of section 4.8 of the summary of product characteristics in order to add the adverse reactions fungal infections, pneumocystis jirovecii pneumonia, bronchopulmonary aspergillosis, systemic candida, viral infection, herpes zoster, influenza, hepatitis B reactivation and cytomegalovirus colitis with a frequency unknown. 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 irinotecan (except for liposomal formulations) the CMDh is of the opinion that the benefit-risk balance of the medicinal product(s) containing irinotecan (except for liposomal formulations) 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 irinotecan (except for liposomal formulations) 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(s) should be added as follows]*

**POST-MARKETING SURVEILLANCE**

| MedDRA System Organ Class | Preferred Term |
|---|---|
| Infections and infestations | • Pseudomembranous colitis one of which has been documented bacteriologically (Clostridium difficile)<br>• Sepsis<br>• **Fungal infections** [a]<br>• **Viral infections** [b] |

***a. e.g. Pneumocystis jirovecii pneumonia, bronchopulmonary aspergillosis, systemic candida.***

***b. e.g. Herpes zoster, influenza, hepatitis B reactivation, cytomegalovirus colitis.***

**Package Leaflet**

**4. POSSIBLE SIDE EFFECTS**

Frequencies from post-marketing surveillance are not known (frequency cannot be estimated from the available data)

*[...]*

- **Fungal infections**
- **Viral infections**

## Annex III

## Timetable for the implementation of this position

**Timetable for the implementation of this position**

| | |
|---|---|
| Adoption of CMDh position: | January 2018 CMDh meeting |
| Transmission to National Competent Authorities of the translations of the annexes to the position: | 10 March 2018 |
| Implementation of the position by the Member States (submission of the variation by the Marketing Authorisation Holder): | 09 May 2018 |