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 paclitaxel, the scientific conclusions of the CHMP are as follows:
Neuropathy is a known ADR with the use of paclitaxel. Review of the post-marketing data revealed that neuropathy can persist after discontinuation of paclitaxel treatment. Data from published literature and administrative claims databases confirmed the persistence of neuropathy with paclitaxel exposure beyond 12 months. Based on the data provided, it is recommended to update the current information on neuropathy in the SmPC, by adding information concerning persistent neuropathy after paclitaxel discontinuation.
Based on a cumulative review of data from all the MAHs, the causal role of paclitaxel for palmar-plantar erythrodysesthesia syndrome is at least a reasonable possibility. From the cases of palmar-plantar erythrodysesthesia syndrome and symptoms received by the MAHs, there were several cases with a positive dechallenge and with a positive rechallenge. In addition, palmar-plantar erythrodysesthesia syndrome associated with paclitaxel treatment has been reported in clinical trials and in the published literature. Therefore, the SmPC of paclitaxel should be updated with the inclusion of palmar-plantar erythrodysesthesia syndrome as an ADR in section 4.8 under SOC Skin and subcutaneous tissue disorders. A frequency of 'not known (cannot be estimated from available data)' is considered appropriate. The PL should be updated accordingly.
The CHMP 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 paclitaxel the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing paclitaxel is unchanged subject to the proposed changes to the product information.
The CHMP recommends that the terms of the marketing authorisation(s) should be varied.

Annex II
Amendments to the product information of the nationally authorised medicinal product(s)

Amendments to be included in the relevant sections of the Summary of Product Characteristics (new text **underlined and in bold**, deleted text strike through)

Section 4.8

The following phrase should be included as a footnote of the ADR 'neuropathy' in the table listing adverse reactions:

***Can persist beyond 6 months of paclitaxel discontinuation**

The following sentence should be included in the text describing nervous system disorders under the section 4.8:

Further, it has been demonstrated that peripheral neuropathies can persist beyond 6 months of paclitaxel discontinuation.

The following adverse reaction should be added under the SOC Skin and subcutaneous tissue disorders with a frequency "not known" (cannot be estimated from available data):

"Palmar-plantar erythrodysesthesia syndrome*"

***As reported in the post marketing surveillance of paclitaxel.**

In addition, the introductory sentence to the table listing adverse reactions is to be amended to reflect that it includes adverse reactions from post marketing experience, as appropriate:

Table X lists adverse reactions (…) observed in (a) clinical study(ies) **and adverse reactions from post-marketing experience. The latter ones may be attributed to paclitaxel regardless of the treatment regimen.**

Amendments to be included in the relevant sections of the Package Leaflet (new text **underlined and in bold**, deleted text strike through)

Section 4

[Existing text may vary between products]

Very common (may effect more than 1 in 10 people)

- Numbness, tingling or weakness in arms and legs (all symptoms of peripheral neuropathy)*

***Can persist beyond 6 months of paclitaxel discontinuation**

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

- redness and swelling of the palms of your hands or soles of your feet which may cause your skin to peel