Annex IV

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 osimertinib, the scientific conclusions of CHMP are as follows:
Six cases of Stevens-Johnson Syndrome (SJS) were identified by the MAH, and while some cases have limitations or are confounded by concomitant medications, there is a positive temporal relationship between the start of treatment with osimertinib and the onset of the event (when reported). Considering the possibility of a class effect, the seriousness of the event of SJS and the importance of early recognition and prompt discontinuation of suspected medication and medical intervention, it is recommended to update the Product Information to include SJS in the list of ADRs and to introduce a relevant warning.
The MAH has provided a review of cases of reoccurrence of osimertinib-related Interstitial lung disease (ILD) when osimertinib was either reintroduced or not discontinued. The provided review led to the conclusions that some patients do benefit from reintroduction of osimertinib therapy. ILD is a known risk for other class products approved for NSCLC indication with a recommendation for discontinuation in case of ILD but not for "permanent" discontinuation. Considering the possible efficacy advantages of osimertinib and that other alternative therapies (including chemotherapy) also carry the risk of ILD toxicity with inferior efficacy, the Product Information should be updated to remove the recommendation for permanent discontinuation of osimertinib and to instead allow the possibility for reintroduction of osimertinib.
As requested, the MAH provided information on cardiac failure related to osimertinib. More data is necessary in order to firmly establish a causal relationship between osimertinib and cardiac failure/decreased cardiac contractility and this remains an important potential risk for osimertinib. However, in view of the accumulating evidence, the statement in section 4.4 of the SmPC 'Based on the available clinical trial data, it is not possible to determine a causal relationship between effects on changes in cardiac contractility and TAGRISSO' should be removed.
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 osimertinib the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing osimertinib 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.