

ANNEX IV
CONDITIONS OF THE MARKETING AUTHORISATIONS

Conditions of the Marketing Authorisations

The following conditions in relation to post-marketing surveillance, studies and review and communication shall be fulfilled by the Marketing Authorisation Holders of nimesulide containing medicinal products (systemic formulation).

Post-marketing surveillance

The MAHs should strengthen the medical review, refine the monitoring of reporting rates, and improve the quality of Individual Case Safety Reports of nimesulide.

The MAHs should expedite and submit all safety reports and case series in PSURs for nimesulide, with a six monthly periodicity. These PSURs should include a specific overview of the hepatic reactions. Hepatic reactions should be given cumulatively and for the period covered by the PSUR. Particular attention should be given to indication, dosage and duration of treatment. These PSURs should be submitted to the National Competent Authorities for assessment.

Studies and Reviews

- The MAHs should conduct a pre-clinical study on identification of reactive metabolites and protein adduct information.
- The MAHs should conduct a review of epidemiological data to review the risk of hepatic damage from nimesulide in comparison with other NSAIDs
- The MAHs should conduct a retrospective cohort study in transplant centres. This study should address the relative risk of nimesulide in respect to other NSAIDs to cause severe hepatic reactions leading to transplants. This retrospective study should lead to a follow-up prospective study in transplant centres. The protocol should be submitted to the CHMP by 3 months after the completion of the final study report of the retrospective study for review and agreement.

The final study reports of the above studies should be submitted to the National Competent Authorities for assessment.

Communication

- The MAHs should submit a revised Risk Management Plan for nimesulide, considering the comments raised during this procedure, to the CHMP. Further updates of the Risk Management Plan should be submitted for assessment at national level.
- The MAHs should inform healthcare professionals on the outcome of this review on nimesulide via a “Direct Healthcare Professional Communication” (DHPC) to be agreed with the CHMP. The communication shall include comprehensive information on the safety risks associated with the use of nimesulide. The draft DHPC should be submitted to the CHMP within one month after adoption of the Commission Decision.
- The MAHs should perform a monitoring activity to evaluate the effectiveness of risk communication on nimesulide. A report should be provided to the National Competent authorities for assessment every 6 months as part of the PSUR (starting within one semester after adoption of the Commission Decision).
- The MAHs should perform a survey to clarify the modes of use of nimesulide in selected EU Member States to identify potential misuse. A report should be provided to the National

Competent authorities for assessment within one year after adoption of the Commission Decision.