Office of Drug Evaluation V
Director Memorandum

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Subject: NDA 20-905 Advisory Committee Meeting March 5, 2003

Date: February 5, 2003

ARAVA (leflunomide), approved as a priority NDA in September 1998, is indicated in adults for the treatment of active rheumatoid arthritis (RA) to reduce signs and symptoms and to retard structural damage as evidenced by X-ray erosions and joint space narrowing. Prior to its approval, this NDA was brought to the Arthritis Advisory Committee in August 1998 for committee review and recommendations on Agency questions. Based on its review and deliberations, the committee unanimously recommended approval for the relief of the signs and symptoms of rheumatoid arthritis and the retardation of structural damage of RA.

Of particular relevance to this committee meeting is the re-visiting of the claim for the prevention of disability. The previous committee discussed disability and considered the issue of claims for "improvement of physical function". The August 1998 Committee deferred recommendation on an improvement of function claim due to the absence of two year data as recommended in the RA Guidance document. In follow-up, the sponsor has submitted additional data to be addressed at this committee meeting.

In light of the safety issues addressed in the 1998 committee meeting and incorporated in the approved labeling, the Agency has provided to the Committee reviews analyzing trends in adverse events associated with the clinical use of Arava. The committee's guidance is sought in assessing clinical risk to benefit and hepatotoxicity as well as identification of opportunities to further improve risk management and to optimize overall conditions of safe use.