BACKGROUND INFORMATION ON THE PROCEDURE

1. Submission of the dossier

The company Merck Sharp & Dohme Ltd, Hertford Road, Hoddesdon Hertfordshire EN11 9BU, United Kingdom submitted on 1 March 1996 an application for Marketing Authorisation to the EMEA for Crixivan capsules 200 mg and 400 mg, through the centralised procedure. After agreement by the CPMP on 21-22 November 1995, this medicinal product was referred to List B in the Annex of the Council Regulation EEC No 2309/93; indent 7, as it contains a new active substance.

The Rapporteur and Co-Rapporteur appointed by the CPMP were:
Rapporteur: Prof. K. Strandberg Co-Rapporteur: Dr. H. Pittner

Licensing status:

Crixivan has received a Marketing Authorisation in several non-EU countries including the United States on 13 March 1996 and in Brazil on 1 April 1996.

2. Steps taken for the assessment of the product

- An application for Marketing Authorisation for Crixivan was submitted to the EMEA on 1 March 1996. The procedure started on 13 March 1996.
- During the April CPMP Meeting 1996, it was agreed to perform a Good Manufacturing Practice inspection on the American manufacturing facility (USA, Virginia) for the finished medicinal product.
- The preliminary clinical Rapporteur's assessment report was circulated to all CPMP Members on 15-18 April 1996.
- The preliminary clinical Co-Rapporteur's assessment report was circulated on 15-18 April 1996.
- The Co-Rapporteur's initial assessment report was circulated to all CPMP Members on 23 April 1996. The Rapporteur's initial assessment report was circulated to all CPMP Members on 26 April 1996.
- An inspection of the manufacturing site (Merck Manufacturing Division, Elkton, Virginia, USA) of the finished medicinal product was carried out by the Health Inspectorate for Medicines, the Netherlands, on 23-25 April 1996.
- A break-out session between the Rapporteur's and the Co-Rapporteur's assessment teams was held on 20 May 1996 to prepare the consolidated list of questions.
- The CPMP consolidated list of questions was sent to the company on 22 May 1996.
- The responses to the consolidated list of questions were provided on 31 May 1996.
- The joint Rapporteur and Co-Rapporteur's assessment report on the responses provided by the applicant was sent to all CPMP Members on 6 June 1996.
- A hearing with the applicant was held on 18 June 1996 during the June CPMP meeting to address the strategy of ongoing clinical studies.
- The applicant submitted on 19 June 1996 their letter of commitments for providing information on clinical aspects as part of the reassessment of the benefit/risk profile. The applicant agreed to provide additional information regarding quality aspects.
- The CPMP, in the light of the overall data submitted and the scientific discussion held within the Committee, issued on 20 June 1996 a positive opinion for granting a Marketing Authorisation for Crixivan.

- Following a rapid alert from France on 14 June 1996 drawing attention to reports of spontaneous bleeding in haemophiliac patients involved in the "compassionate use (Autorisation Temporaire d'Utilisation)" programme, the CPMP, during its meeting of 16-17 July 1996 agreed to revise the opinion adopted on 20 June 1996. In the revised opinion warnings have been introduced into the Summary of Product Characteristics and in the Package Leaflet in the light of the information available. The wordings proposed by the CPMP have been discussed between the Chairman of the Committee and the companies involved in the marketing of protease inhibitors. An agreement on the warnings to be introduced was reached on Monday 22 July 1996.
- The CPMP revised opinion was forwarded in all official languages of the European Union to the European Commission, which adopted the corresponding Decision on 4 October 1996.