STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 1 November 2003 please refer to module 8B**.**

- On 3 December 1999 the Marketing Authorisation Holder submitted a Type II variation application in accordance with Article 6 of Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of the variation related to a change in the specifications for the active ingredient/DNA content.

  On 16 February 2000 the CPMP approved the variation. The corresponding Commission Decision was issued on 11 May 2000.

- The Marketing Authorisation Holder submitted to the EMEA on 17 May 2000 an application for a Type I variation falling within the scope of item No 24 of Annex I to Commission Regulation (EC) No 542/95. The Marketing Authorisation Holder applied for a change in the test procedure for the active substance/system.

  On 16 June 2000 the EMEA approved the variation. The corresponding Commission Decision was issued on 24 July 2000.

- On 7 February 2000 the Marketing Authorisation Holder submitted a Type II variation application in accordance with Article 6 of Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of the variation related to an update of the SPC in the light of additional clinical experience.

  On 24 May 2000 the CPMP approved the variation. The variation required amendments in the relevant sections of the Commission Decision. The European Commission amended the Decision on 28 August 2000.

- The Marketing Authorisation Holder submitted to the EMEA on 22 June 2000 an application for a Type I variation falling within the scope of item No 20 of Annex I to Commission Regulation (EC) No 542/95; extension of shelf life from 18 to 24 months.

  On 21 July 2000 the EMEA approved the variation. The corresponding Commission Decision was issued on 12. September 2000.

- The Marketing Authorisation Holder submitted to the EMEA on 14 June 2000 an application for a Type I variation falling within the scope of item No 31 of Annex I to Commission Regulation (EC) No 542/95. The Marketing Authorisation Holder applied for a change in container shape.

  On 21 July 2000 the EMEA approved the variation. The corresponding Commission Decision was issued on 2 October 2000.

- The Marketing Authorisation Holder submitted to the EMEA on 14 June 2000 an application for a Type I variation No 1 of Annex I to the regulation and a consequential application for a Type I variation No 15 related to addition of a new manufacturing site for the finished product (Roche, Basel) and minor changes in manufacture of the medicinal product.

- On 27 July 2000 the CPMP approved the variation. This variation did not require amendments to the Commission Decision.

Subsequent post Marketing Authorisation applications agreed upon are summarised in the table below:

Scope	Application number	Type of modification[1]	Notification/ Opinion issued on[2]	Commission Decision Issued/amended on
Change to the primary packaging of the product; change in the rubber stopper type	II-0007	II	14.12.00	20.02.01
Demonstration of compliance with the Commission Directive 1999/82/EC and the Note for Guidance on Minimising the risk of transmitting animal spongiform Encephalopathy agents via medicinal products.	II-0008	II	26.04.01	
Change in the manufacture site of the active ingredient	I-0009	I	26.07.01	26.07.01
Extension of the therapeutic indication to include paedriatic patients up to 17 years old and changes in the Package Leaflet to be in accordance with the EMEA QRD templates	II-0011	II	21.02.02	24.05.02
Changes affecting the labelling layout and text to comply with the EMEA QRD template.	N-0012	I	30.07.02	06.08.02
Deletion of a sentence in section 4 of the Package Leaflet and minor linguistic change incorporated in section 2 of the Portuguese text to bring it in line with more accurate usage for that market. Other changes included in the local representatives address list.	N-0014	I	10.03.03	16.04.03
Amendment to section 5.1 (Pharmacodynamic properties) of the SPC and section 2 of the PL of Zenapax, with respect to the results of study NR15880 evaluating the efficacy and the safety of daclizumab in combination with immunosuppressive therapy, which includes mycophenolate mofetil, cyclosporine and steroids, in patients undergoing cardiac transplantation.	II-0015	II	24.07.03	20.10.03
Amendment to section 5.1 (Pharmacodynamic properties) of the SPC, as requested by the CPMP further to the assessment of the additional data requested following the review of PSUR 5 (01.01.01 - 31.12.01), to include the three-year follow-up data from registration trials NO14393 and NO14874 where Zenapax was used in combination with standard two- or three-drug immunosuppressive therapy for prevention of acute allograft rejection in recipients of first cadaver renal transplants.	II-0016	II	24.07.03	20.10.03

[1] In accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended: **I** refers to a minor variation (Type I variation); **II** refers to a major variation (Type II variation); **I/II** refers to a minor variation following the procedure set out in Article 6, 7 and 8 of the Regulation; **X** refers to an Annex II application.
T refers to a transfer of a Marketing Authorisation in accordance with Commission Regulation (EC) No 2141/96 of 7 November 1996.
N refers to a notification in accordance with Article 10(3) of Council Directive 92/27/EEC of 31 March 1992.

[2] For Notifications and Type I variations, the date of entry into force of the change is the EMEA Notification date. The Commission Decision will be amended accordingly.