STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 1 February 2001 please refer to module 8B.

- On 17 August 1998 the Marketing Authorisation Holder submitted to the EMEA nine applications for Type I variations (I/01-09) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. These variations were related to changes in the qualitative composition of the immediate packaging material, a change in the batch size of the finished product, an extension of the retest period of the active substance and minor changes of the manufacturing process of the active substance. The variations were approved by the EMEA on 23 September 1998 and did not require any amendments to the Commission Decision.
- On 8 January 1999 the Marketing Authorisation Holder submitted to the EMEA five applications for Type I variations (I/10-14) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. These variations were related to a change in the manufacturing authorisation and to changes in the test procedures of the active substance. The variations were approved by the EMEA on 8 February 1999 and did not require any amendments to the Commission Decision.
- On 14 June 1999 the Marketing Authorisation Holder submitted to the EMEA an application for a Type II variation (II/15) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. This application was related to the update of the Summary of Product Characteristics (SPC) and of the Package Leaflet on the basis of the results of interaction studies performed with compounds inhibiting or inducing CYP 3A4. Repaglinide ATC code was also changed from A10B H01 to A10X02. The CPMP adopted on 23 September 1999 a positive Opinion on this Type II variation and the European Commission amended the Decision on 20 January 2000
- On 15 September 1999 the Marketing Authorisation Holder submitted to the EMEA five applications for Type I variations (I/17-21) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. These variations were related to changes to extend the retest period of the active substance, to changes in in-process controls applied during the manufacture, to a change in the test procedure of the active substance and to an extension of the shelf life. These variations were approved by the EMEA on 20 October 1999. Four of these variations did not require any amendments to the Commission Decision, and one of them (extension of the shelf life) required an amendment to the SPC. The European Commission amended the Decision on 13 December 1999.
- On 2 November 1999 the Marketing Authorisation Holder submitted to the EMEA an application for a Type II variation (II/22) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to change the manufacturing site of the active substance and a change in the manufacturing process. The CPMP adopted on 19 January 2000 an Opinion on this Type II variation and a favourable Decision was issued by the European Commission on 22 February 2000.
- On 28 March 2000 the Marketing Authorisation Holder submitted to the EMEA three applications for Type I variations (I/23-25) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. These variations were related to changes in the test procedures of the medicinal product and to a change in the specifications of the medicinal product. The variations were approved by the EMEA on 26 April 2000 and did not require any amendments to the Commission Decision.
- On 8 September 2000 the Marketing Authorisation Holder submitted to the EMEA an application for a Type II variation (II/26) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to update the SPC (section 4.3) and Package Leaflet based on the results of a renal efficacy and safety study and to update the SPC (section 4.8) and Package Leaflet with regards to information on hepatic dysfunction. The CPMP adopted on 16 November 2000 an Opinion on this Type II variation and a favourable Decision was issued by the European Commission on 5 March 2001.

- On 5 October 2000 the Marketing Authorisation Holder submitted to the EMEA four applications for Type I variations (I/27-30) in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. These variations were related to extension of the shelf life, change in the container shape, change in the qualitative composition of immediate packaging material, and change of the manufacturing site for part or all of the manufacturing process of the medicinal product. These variations were approved by the EMEA on 7 November 2000. Three of these variations did not require any amendments to the Commission Decision, and one of them (extension of the shelf life) required an amendment to the SPC. The European Commission amended the Decision on 22 January 2001.