STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

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

- In accordance with Article 10(3) of Council Directive 92/27 EEC of 31 March 1992, the EMEA issued on 9 March 1999 a notification for amendment in the labelling text for the blister foil in all official languages. The respective Commission Decision was issued on 11 May 1999.
- On 6 November 1998 the Marketing Authorisation Holder (MAH) submitted an application for a type II variation relating to an update of section 4.5 of the SPC and the relevant section of the PL concerning the interaction of Xenical with pravastatin. The CPMP adopted a positive opinion on 27 January 1999. The respective Commission Decision was issued on 11 May 1999.
- On 27 November 1998 the MAH submitted an application for a type I variation relating to an additional manufacturer of the finished product in Nutley, New Jersey, USA. The procedure started on 17 December 1998. This variation was approved by the EMEA on 13 January 1999 and did not require any amendments to the Community Marketing Authorisation.
- On 20 January 1999 the MAH submitted an application for a type I variation relating to three additional manufacturers of the active substance, as well as an additional milling site for the active substance. A change in the address of the existing milling site is introduced as well. The procedure started on 1 February 1999. This variation was approved by the EMEA on 26 February 1999 and did not require any amendments to the Community Marketing Authorisation.
- On 5 March 1999 the MAH submitted an application for two type I variations relating to modifications of the analytical methods for the active substance. The procedure started on 12 March 1999. These variations were approved by the EMEA on 13 May 1999 and did not require any amendments to the Community Marketing Authorisation.
- On 5 March 1999 the MAH submitted an application for a type I variation relating to a change to the visual control and weight control of the capsule. The procedure started on 12 March 1999. This variation was approved by the EMEA on 31 March 1999 and did not require any amendments to the Community Marketing Authorisation.
- On 16 March 1999 the MAH submitted an application for a type I variation relating to additional packaging sites. The procedure started on 19 March 1999. This variation was approved by the EMEA on 16 April 1999 and did not require any amendments to the Community Marketing Authorisation.
- On 15 April 1999 the MAH submitted an application for a type I variation relating for a modification of final step in the manufacture of the active substance. The procedure started on 21 April 1999. This variation was approved by the EMEA on 19 May 1999 and did not require any amendments to the Community Marketing Authorisation.
- On 23 April 1999 the MAH submitted an application for a type II variation to include additional information in the relevant parts of the SPC and PL with respect to hypersensitivity reactions reported following PSUR 1. The CPMP adopted a positive opinion on 29 July 1999. The respective Commission Decision was issued on 8 December 1999.
- On 19 October 1999 the MAH submitted an application for a type II variation to include additional information in the relevant parts of the SPC and PL with respect to the concomitant administration of cyclosporin and fibrates with orlistat. The CPMP adopted a positive opinion on 19 January 1999. The respective Commission Decision was issued on 11 May 2000.
- On 29 September 2000, the MAH submitted applications for two type II variations in accordance with Article 6 of the Commission Regulation (EC) 542/95. The MAH applied for an update of the section 4.5 of the SPC and PL to exclude information on the interaction with biguanides based on a pharmacokinetic study, as well as an update of the section 4.8 of the SPC and PL to include information of hepatic disorders based on the PSUR 3. The CPMP adopted a

positive opinion for this variation on 26 January 2001. The respective Commission Decision was issued on 3 May 2001.

- On 12 October 2001 the MAH submitted to the EMEA applications for type I variations in accordance with Article 4 of Commission Regulation (EC) No. 542/95, as amended. The scopes of the variations were to make a minor change of manufacturing process of the active substance and to change the test procedure for a starting material or intermediate used in the manufacture of the active substance. The procedure started on 13 December 2001. The EMEA notified the Commission on 11 January 2002 that the variations were accepted and did not require any amendments to the Community Marketing Authorisation.
- On 19 June 2001, the MAH submitted an application for a type II variation in accordance with Article 6 of Commission Regulation (EC) 542/95 as amended. The MAH applied for an update of sections 4.8 and 5.1 of the SPC to include information regarding the use of Xenical in obese and overweight patients with type 2 diabetes. The CPMP adopted a positive opinion for this variation on 21 March 2002. The respective Commission Decision was issued on 20 June 2002.
- On 10 September 2002, the MAH submitted an application for a type II variation in accordance with Article 6 of Commission Regulation (EC) 542/95 as amended. The MAH applied to update the SPC sections 4.4, 4.5 and 4.8 as requested by the CPMP following the assessment of the 5th Periodic Safety Update Report (PSUR). In addition, amendments were made to the section 4.9 considering post-marketing data and additions to section 4.5 resulting from completed drug-drug interaction studies. The CPMP adopted a positive opinion for this variation on 21 November 2002. The respective Commission Decision was issued on 4 March 2003.
- On 10 March 2003, the MAH submitted an application for a type II variation in accordance with Article 6 of Commission Regulation (EC) 542/95 as amended. The MAH applied for changes to manufacture of the product. The procedure started on 21 March 2003. The CPMP adopted a positive opinion for this variation on 22 May 2003. The variation did not require any amendment to the Community Marketing Authorisation.
- On 16 April 2003, the MAH submitted an application for a type II variation in accordance with Article 6 of Commission Regulation (EC) 542/95 as amended. The MAH applied for an update of section 4.8 of the SPC to include two additional terms as requested by the CPMP following the assessment of PSUR 6. The PL was updated accordingly. The procedure started on 25 April 2003. The CPMP adopted a positive opinion for this variation on 26 June 2003. The respective Commission Decision was issued on 8 October 2003.
- For the first renewal of Xenical, the CPMP was of the opinion that the quality, safety and efficacy of this medicinal product continued to be adequately and sufficiently demonstrated and therefore considered that the benefit/risk profile continued to be favourable for the authorised indications and issued on 26 June 2003 a positive opinion for the renewal of the Community Marketing Authorisation. The respective Commission Decision was issued on 8 October 2003.