STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 1 March 2004 please refer to module 8B

- On 7 March 2000 the MAH submitted to the EMEA an application for a type I variation in accordance with Article 4 of Commission Regulation (EC) No. 542/95, as amended. The scope of this variation was to make a minor change in the manufacturing process of the active substance. The procedure started on 13 March 2000. The EMEA notified the European Commission on 10 April 2000 that the variation was accepted and did not require any amendment to the Community Marketing Authorisation.
- On 21 June 2000, the MAH submitted an application for a type II variation in accordance with Article 6 of Commission Regulation (EC) 542/95 as amended. The scope of the variation was to update the SPC and PL based on the 5th PSUR and a separate review of cases of diabetic ketoacidosis and coma. The CPMP adopted a positive Opinion on 21 September 2000. The respective European Commission Decision was issued on 27 December 2000.
- On 6 December 2000, the MAH submitted an application for a type II variation in accordance with Article 6 of Commission Regulation (EC) 542/95 as amended. The scope of the variation was to update the section 4.8 of the SPC regarding information on hyperglycaemia, and the respective section of the PL to reflect this change. The procedure started on 15 December 2000. The CPMP adopted a positive Opinion on 1 March 2001. The respective European Commission Decision was issued on 14 June 2001.
- On 3 January 2001 the MAH submitted to the EMEA an application for a type I variation in accordance with Article 4 of Commission Regulation (EC) No. 542/95, as amended. The scope of this variation was to demonstrate 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 (CPMP/BWP/1230/98). The procedure started on 5 January 2001. The EMEA notified the European Commission on 2 February 2001 that the variation was accepted and did not require any amendments to the Commission Decision.
- On 19 February 2001 the MAH submitted to the EMEA an application for a type I variation in accordance with Article 4 of Commission Regulation (EC) No. 542/95, as amended. The scope of the variation was to change the address of the MAH. The procedure started on 23 February 2001. The EMEA notified the European Commission on 1 March 2001 that the variation was accepted. Amendments to the Annexes I, IIIA and IIIB were required and the Commission Decision was issued on 14 June 2001.
- On 14 March 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 extension of the therapeutic indication to patients with bipolar disorder suffering from a manic episode. The CPMP adopted a positive Opinion on 21 February 2002 for the indication "olanzapine is indicated for the treatment of a moderate to severe manic episode; olanzapine has not been demonstrated to prevent recurrence of manic or depressive episodes". The respective Commission Decision was issued on 4 June 2002.
- On 22 May 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 the SPC, labelling and PL to maintain consistency of the texts following the 5-year renewal application for Zyprexa. The procedure started on 1 June 2001. The CPMP adopted a positive Opinion on 26 July 2001. The respective Commission Decision was issued on 20 November 2001.
- On 1 March 2002, the MAH submitted to the EMEA an application for a type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The procedure started on 15 March 2002. The scope of this variation was to add a new packaging site and rename an authorised packaging site. The EMEA notified the European Commission on

15 April 2002 that the variation was accepted and did not require any amendment to the Community Marketing Authorisation.

- On 12 February 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 procedure started on 22 February 2002. The MAH applied for an update of the SPC sections 4.8 and 4.5 and the corresponding sections of the PL following the 7th PSUR. The procedure started on 22 February 2002. The CPMP adopted a positive Opinion on 30 May 2002. The respective Commission Decision was issued on 10 September 2002.
- Pursuant to article 61(3) of Council Directive No. 2001/83/EC of 6 November 2001, the MAH notified the EMEA on 26 September 2002 of their intention to introduce changes to an aspect of the PL not connected to the SPC. On 25 October 2002, the EMEA notified the European Commission that the changes were accepted.
- On 6 December 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 procedure started on 20 December 2002. The application related to an update in section 4.1 of the SPC to extend the therapeutic indication to include prevention of recurrence in patients with bipolar disorder. The CPMP adopted a positive Opinion on 27 July 2003 for the indication "olanzapine is indicated for the prevention of recurrence in patients with bipolar disorder". The respective Commission Decision was issued on 24 October 2003.
- On 4 February 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 procedure started on 24 February 2003. The application referred to an update to section 4.6 of the SPC regarding the levels of olanzapine found in breast milk, as well as section 4.8 regarding EPS following the review of the 9th PSUR. The CPMP adopted a positive Opinion on 26 June 2003. The respective Commission Decision was issued on 8 October 2003.
- On 5 March 2003 the MAH submitted to the EMEA an application for a type I variation in accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended. The scope of this variation was to change the qualitative composition of the immediate packaging material. This variation was accepted by the EMEA on 7 April 2003 and did not require any amendment to the Community Marketing Authorisation.
- On 15 December 2003, the MAH submitted to the EMEA an application for a type I variation in accordance with Annex I (No. IB29A) of Commission Regulation (EC) No. 1085/2003. The scope of this variation was for an alternative composition of the aluminium blister and the foil backing for the aluminium blister. This variation was accepted by the EMEA on 12 January 2004.
- On 4 February 2004, the MAH submitted to the EMEA an application for a type I variation in accordance with Annex I (No. IA47a) of Commission Regulation (EC) No. 1085/2003. The scope of this variation was to change the name of the manufacturing, control testing and primary packaging site. This variation was accepted by the EMEA on 9 February 2004.
- On 1 March 2004, an Urgent Safety Restriction procedure was started at the request of the MAH to include information on cerebrovascular adverse events and increased mortality in elderly patients with dementia. The procedure was finalised on 2 March 2004.