STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 30 November 2004 please refer to module 8B.

- On 21 July 1999 the Marketing Authorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95. The scope of the variation related to the inclusion of an additional batch size of the finished product. This variation did not require any amendment to the terms of the Community Marketing Authorisation.
- On 21 July 1999 the Marketing Authorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) No. 542/95. The scope of the variation related to a change in manufacturing site for part or all of the manufacturing process of the medicinal product. The EMEA approved the variation on 12 August 1999, which required amendments to be incorporated in the relevant sections of the Commission Decision. The European Commission amended the Decision on 5 October 1999.
- Pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended, Norton Healthcare Limited submitted to the EMEA on 13 April 2000 an application for a Type I variation. The procedure started on 19 April 2000. The scope of the variation related to a change of manufacturing site. This variation did not require any amendment to the terms of the Community Marketing Authorisation. The Notification was signed by the EMEA on the 15 May 2000.
- Pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended, Norton Healthcare Limited submitted to the EMEA on 9 November 1999 an application for a Type II variation. The procedure started on 19 November 1999. Supplementary information was supplied by the Marketing Authorisation Holder on 14 January 2000 and a clarification on the supplementary information was supplied on 14 April 2000. The scope of the variation related to an application for the addition of a manufacturer of the active ingredient. This variation did not require any amendments to the terms of the Community Marketing Authorisation. The EMEA approved the variation on the 25 May 2000.
- Pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended, Norton Healthcare Ltd submitted to the EMEA on 15 June 2000 an application for a Type II variation. The procedure started on 30 June 2000. The scope of the variation related to amendment to section 4.8 of the SPC following the review of the first PSUR for Paxene. The EMEA approved the variation on the 27 July 2000, which required amendments to be incorporated in the relevant sections of the Commission Decision. The European Commission amended the Decision on 14 November 2000.

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
Update of Summary of Product Characteristics	II/06	II	18.10.01	08.10.02
Update of Summary of Product Characteristics (point 4.5)	II/07	II	28.05.02	08.10.02
Extension of Indication	II/08	II	21.01.04	08.03.04
Extension of Indication	II/09	II	21.01.04	08.03.04
Quality changes	II/10	II	21.01.04	30.01.04
Change in the batch size of finished product	I/11	I	26.11.03	-
New presentation(s)	II/12	II	20.11.03	20.01.04
Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	IA/14	IA	26.03.04	-
Minor change in the manufacturing process of the active substance	IB/16	IB	22.04.04	-
Change in re-test period of the active substance	IB/17	IB	14.04.04	-
Change in the name and/or address of a manufacturer of the finished product	IA/18	IA	26.03.04	-
Change in BR/QC testing - repl./add. manuf. responsible for BR - incl. BC/testing	IA/19	IA	31.03.04	-
Change in spec. of active subst./agent in manuf. of active subst. - test parameter	IB/21	IB	19.07.04	
Renewal	R/22	R	29.07.04	28.10.04
Quality changes	II/23	II	18.11.04	25.11.04
Replacement/add. of manufacturing site: Secondary packaging site	IA/29	IA	14.10.04	-
Change in any part of primary packaging material not in contact with finished product	IA/30	IA	11.10.04	-

[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.