**Steps taken after granting the Marketing Authorisation**

**For procedures finalised after 1 September 2004 please refer to module 8B.**

- The Marketing Authorisation Holder submitted to the EMEA on 06 November 1998 an application for one type I variation falling within the scope of item No 3 of Annex I to Commission Regulation (EC) No 542/95, as amended. The Marketing Authorisation Holder applied for:
  A change in the address of the marketing authorisation holder.
  On 03 December 1998, the EMEA approved the variation. The variation required amendments in the relevant sections (annexes I, IIIA and IIIB) of the Commission decision. The European Commission amended the Decision on 01 February 1999.

- The Marketing Authorisation Holder submitted to the EMEA on 29 December 1998 an application for one type I variation falling within the scope of item No 8 of Annex I to Commission Regulation (EC) No 542/95, as amended. The Marketing Authorisation Holder applied for:

  A change in the qualitative composition of immediate packaging material.

  On 05 February 1999, the EMEA approved the variation. This variation required amendments to annexes I and IIIB of the Commission Decision. Revised EMEA notification dated 01 April 1999 regarding EU numbers. The European Commission amended the Decision on 11 June 1999.

- The Marketing Authorisation Holder submitted to the EMEA on 04 February 1999 an application for one type I variation falling within the scope of item No 1 of Annex I to Commission Regulation (EC) No 542/95, as amended. The Marketing Authorisation Holder applied for:

  An alternative manufacturing site for the finished product.

  On 22 March 1999, the EMEA approved the variation. This variation required amendments to annexes II and IIIB of the Commission Decision. The European Commission amended the Decision on 16 July 1999.

- The Marketing Authorisation Holder submitted to the EMEA on 04 February 1999 an application for one type I variation falling within the scope of item No 16 of Annex I to Commission Regulation (EC) No 542/95, as amended. The Marketing Authorisation Holder applied for:

  A change in the batch size of the finished product.

  On 22 March 1999, the EMEA approved the variation. This variation did not require any amendment to the Commission Decision.

- The Marketing Authorisation Holder submitted to the EMEA on 08 April 1999 an application for one type I variation falling within the scope of item No 32 of Annex I to Commission Regulation (EC) No 542/95, as amended. The Marketing Authorisation Holder applied for:

  A new engraving on the tablets.

  On 13 May 1999, the EMEA approved the variation. This variation required amendments to annexes I and IIIB of the Commission Decision. The European Commission amended the Decision on 08 July 1999.

- The Marketing Authorisation Holder submitted to the EMEA on 08 April 1999 an application for one type I variation falling within the scope of item No 14 of Annex I to Commission Regulation (EC) No 542/95, as amended. The Marketing Authorisation Holder applied for:

  A change in specifications of the active substance.

  On 06 July 1999, the EMEA approved the variation. This variation did not require any amendment to the Commission Decision.

- On 26 April 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 the update of the Summaries of Product Characteristics and Package Leaflets according to the assessment of the second PSUR

  On 20 May 1999 the CPMP approved the variation. The variation required amendments in annexes I and IIIB of the Commission Decision. The European Commission amended the Decision on 07 September 1999.

- Between 31 August 1999 and 4 May 2000, the EMEA issued Notifications for the approval of five type I variations concerning

  - change in the manufacturer of the active substance,
  - change in the batch size of the active substance,
  - minor change of manufacturing process of the active substance,
  - change in the manufacturer of the active substance,
  - change of the manufacturing site for part of the manufacturing process of the medicinal product.

  These variations did not require any amendment to the Commission decision.

- On 10 February 2000, the Marketing Authorisation Holder requested to update names and adresses of local representatives in the package leaflet, by means of a Notification under Article 10(3) of Directive 92/27/EEC. Following EMEA's Notification on 10 March 2000, the European Commission amended the Decision (Annex IIIB) on 03 May 2000.

- On 07 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 the update of the Summaries of Product Characteristics according to the assessment of the fourth PSUR. On 12 April 2000 the CPMP approved the variation. At the same time, annex II of the Commission Decision has been updated. The variation required amendments in annexes I and II of the Commission Decision. The European Commission amended the Decision on 13 July 2000.

- On 15 May 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 Marketing Authorisation Holder applied for a new formulation of the film-coated tablet containing a new polymorphic form of the active substance. In addition to the subsequent changes in the SPC, Labelling and PL, these annexes have been revised according to the latest templates. On 21 September 2000 the CPMP approved the variation. The variation required amendments in annexes I, IIIA and IIIB of the Commission Decision. The European Commission amended the Decision on 15 January 2001.

- On 26 July 2000, the Marketing Authorisation Holder requested to introduce changes to an aspect of the labelling not connected to the Summary of Product Characteristics, by means of a Notification under Article 10(3) of Directive 92/27/EEC. Following EMEA's Notification on 1 August 2000, the European Commission amended the Decision (Annex IIIA) on 25 September 2000.

- On 5 September 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 Marketing Authorisation Holder applied for an update of the SPC following the assessment of a PSUR. On 16 November 2000 the CPMP approved the variation. The variation required amendments in annexes I and IIIB of the Commission Decision. The European Commission amended the Decision on 13 March 2001.

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 (sections 4.4, 4.5 and 4.8) andPackage Leaflet following the assessment of the 5th PSUR. | II/18 | II | 29.03.01 | 16.07.01 |
| Batch size of active substance | I/19 | I | 04.03.01 | N/A |
| Minor change of manufacturing process of the active substance | I/20 | I | 04.03.01 | N/A |
| Change in or addition of manufacturer(s) of active substance | I/21 | I | 19.07.01 | N/A |
| Update of the Summary of Product Characteristics and Package Leaflet | II/22 | II | 23.08.01 | 28.01.02 |
| Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | N/23 | N | 08.10.01 | 17.12.01 |
| Additional indication (Acute Coronary Syndrome) | II/24 | II | 28.05.02 | 09.09.02 |
| Change following modification(s) of the manufacturing authorisation | I/25 | I | 13.12.01 | 19.02.02 |
| Change in or addition of manufacturing site(s) for part or all of the manufacturing process | I/26 | I | 16.05.02 | 19.06.02 |
| Change in the name of a manufacturer of the medicinal product | I/27 | I | 27.05.02 | 27.05.02 |
| Extension of shelf-life as foreseen at time of authorisation | I/28 | I | 20.12.02 | 03.02.03 |
| Change in test procedure for starting material/intermediate used in manuf. of active substance | I/29 | I | 19.02.03 | 03.03.03 |
| Batch size of active substance | I/30 | I | 10.01.03 | 16.01.03 |
| Change in the batch size of finished product | I/31 | I | 27.03.03 | 01.04.03 |
| Minor changes in manufacture of the medicinal product | I/32 | I | 27.03.03 | 01.04.03 |
| Change in pack size for a medicinal product | I/33 | I | 14.02.03 | 24.03.03 |
| Change in pack size for a medicinal product | I/34 | I | 14.02.03 | 24.03.03 |
| Renewal | R/35 | R | 22.05.03 | 08.10.03 |
| Change(s) to the manufacturing process for the active substance | II/36 | II | 25.09.03 | 02.10.03 |
| Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | N/37 | N | 20.11.03 | 22.12.03 |
| Update of Summary of Product Characteristics and Package Leaflet | II/38 | II | 03.06.04 | 02.08.04 |
| Replacement/add. of manufacturing site: Secondary packaging site and change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing | IA/39 | IA | 11.06.04 | - |

[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.