Steps taken after granting the Marketing Authorisation

For procedures finalised after 5 September 2004 please refer to module 8B.

- On 28 May 1999, the Marketing Authorisation Holder submitted to the EMEA two applications for a Type I variation. The first application related to the inclusion of an alternate manufacturing site for ribavirin capsules and the second application related to a minor change of manufacturing process of the active substance. The EMEA approved these variations on 7 July 1999.

- On 18 February 2000, the Marketing Authorisation Holder submitted to the EMEA an application for a Type I variation related to a minor change of manufacturing process of the active substance. The EMEA approved this variation on 24 March 2000.

- On 5 January 2000, the Marketing Authorisation Holder submitted to the EMEA an application for a Type II variation related to the update of the Summary of Product Characteristics and Package Leaflet to include two undesirable effects. The CPMP, during its March plenary meeting, considered the changes acceptable, and adopted on 16 March 2000 a favourable opinion on the Type II variation. The corresponding Commission Decision was issued on 24 July 2000.

- On 9 June 2000, the Marketing Authorisation Holder submitted to the EMEA an application for a Type II variation related to the extension of the indication for ribavirin to be used in combination with peginterferon alfa-2b for the treatment of chronic hepatitis C.
  The CPMP, during its December plenary meeting, considered the changes acceptable, and adopted on 14 December 2000 a favourable opinion on the Type II variation. The corresponding Commission Decision was issued on 26 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
Extension of indication to use ribavirin in combination with peginterferon alfa-2b for the treatment of chronic hepatitis C.	II/0005	II	14.12.00	26.03.00
Quality change (to comply with European TSE Directive and Guidance)	II/0006	II	25.04.01	-
Minor change of Manufacturing process.	I/0007	I	02.03.01	-
The Marketing Authorisation Holder applied for the addition in the labelling of information on the sustained response rate from the pivotal trial with combination therapy (C/I98-580) in patients with baseline fibrosis. Moreover the information with regard to mitochondrial toxicity and lactic acidosis reported in HIV-positive patients receiving NRTI regimen and co-infected with HCV/HBV has been also included in the SPC through this variation.	II-0008	II	15.11.01	12.04.02
Quality change (in in-process control specifications)	II-0009	II	18.10.01	-
This notification relates to address changes affecting the Package Leaflet (Annex IIIB).	N-0010	N	22.10.01	07.02.02

[1] In accordance with Commission Regulation (EC) No. 542/95 of 10 March 1995, as amended for procedures finalised before 1 October 2003. In accordance with Article 6 of Commission Regulation (EC) No 1085/2003 for procedures finalised after 1 October 2003 : **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.

The MAH applied to add a stand-alone checkweighter machine to be used after the encapsulation process in order to verify the weight of each capsule and to reject those that are outside of the specification ranges.	I-0012	I	10.04.03	-
The MAH applied to add an alternative encapsulator equipped with an in-line weight verification system.	I-0013	I	10.04.03	-
The MAH applied for an update of Summary of Product Characteristics, to add information on carcinogenicity in sections 4.4 (Special warnings and special precautions for use) and 5.3 (Preclinical safety data) following follow-up measure result of study SCH 18908.	II-0011	II	26.06.03	03.10.03
The MAH applied for a number of changes related to the active substance, ribavirin. These changes involve the synthesis process as well as specifications and test methods. Furthermore, an extension of the shelf life from 1 to 3 years is proposed for ribavirin synthesised by Orgamol (Evionnaz site - Switzerland).	II-0015	II	25.09.03	-
Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	N-0017	N	10.11.03	-
Renewal of the Marketing Authorisation	R-0019	R	22.04.04	02.09.04