Procedural steps taken after granting the Marketing Authorisation

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

- The changes introduced in the revision 1 of this EPAR are editorial amendments to Part III, section 4: Overview of part IV of the dossier: clinical aspects.

- The MAH submitted on 26 March 1997 an application for a Type II variation, in order to apply for the use of NovoSeven also outside of specialized centres, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995. The procedure started on 18 April 1997, supplementary information was supplied by the MAH on 1 July 1997 and a positive opinion was adopted by the CPMP on 23 July 1997. The European Commission granted a Commission decision on 4 December 1997.

- The MAH submitted on 23 July 1997, three applications for three Type I variations No 12 of Annex I, (type II procedure applicable) in order to apply for a change in the manufacture of the bulk product, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedures started on 25 July 1997 and a positive opinion was adopted by the CPMP on 24 September 1997.

- The MAH submitted on 16 April 1998, an application for a Type I variation No 12 of Annex I, (type II procedure applicable) in order to remove the bovine derived Primatone RL from the cultivation process in order to minimise the use of animal derived material, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 24 April 1998 and a positive opinion was adopted by the CPMP on 24 June 1998.

- The MAH submitted on 16 April 1998 an application for a Type II variation, in order to apply for an additional needle for injection, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 24 April 1998, supplementary information was supplied by the MAH on 10 July 1998 and a positive opinion was adopted by the CPMP on 23 July 1998. The European Commission granted a Commission decision on 19 November 1998.

- The MAH submitted on 6 April 1998, an application for a Notification of a Type I variation No 20 of Annex I, in order to change the shelf-life of the finished product, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 16 April 1998 and a positive opinion was adopted by the CPMP on 15 May 1998.

- The MAH submitted on 30 October 1998 an application for a Type II variation, in order to apply for the extension of the storage period/shelf life of bulk product, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 20 November 1998 and a positive opinion was adopted by the CPMP on 27 January 1999.

- The MAH submitted on 30 October 1998 an application for a Type II variation, in order to apply for changes in the bulk product specification, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 20 November 1998 and a positive opinion was adopted by the CPMP on 27 January 1999.

- The MAH submitted on 30 October 1998 an application for a Type II variation, in order to apply for the replacement of the test for pyrogens, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 20 November 1998 and a positive opinion was adopted by the CPMP on 27 January 1999.

- The MAH submitted on 30 October 1998, an application for a Type I variation No 12 of Annex I, (type II procedure applicable) in order to apply for minor changes to the manufacturing

process related to the fermentation and purification processes, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 18 December 1998 and a positive opinion was adopted by the CPMP on 23 February 1999.

- The MAH submitted on 30 October 1998, an application for a Type I variation No 11 of Annex I, (type II procedure applicable) for the addition of an alternative manufacturer of the raw material, pursuant to Article 4 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 18 December 1998 and a positive opinion was adopted by the CPMP on 23 February 1999.

- The MAH submitted on 19 May 1999 an application for a Type II variation at the request of the CPMP following the the evaluation of the 4th and 5th PSUR, in order to modify the SPC and Package Leaflet, pursuant to Article 6 of Commission Regulation (EC) No 542/95 of 10 March 1995 as amended. The procedure started on 21 May 1999, supplementary information was supplied by the MAH on 30 June 1999 and a positive opinion was adopted by the CPMP on 28 July 1999. The European Commission granted a Commission decision on 8 December 1999.

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
Quality changes	II/15	II	19.10.00	28.11.00
Replacement of an excipient with a comparable excipient	I/16	I	15.09.00	12.10.00
Renewal	R/17	R	25/01.01	3.05.01
Update of summary of product characteristics and package leaflet	II/18	II	01.03.01	20.06.01
Changes to comply with supplements to pharmacopoeias	I/19	I	13.03.01	06.04.01
Minor change of manufacturing process of the active substance	I/20	I	25.04.02	29.04.02
Minor change of manufacturing process of the active substance	I/21	I	25.04.02	29.04.02
Synthesis or recovery of non-pharmacopoeial excipients in the medicinal products	I/22	I	15.07.02	15.07.02
Change in test procedure of active substance and Change in test procedures of the medicinal product	I/23	I	21.11.02	09.12.02
Change in the batch size of finished product	I/24	I	20.02.03	10.03.03
Minor changes in manufacture of the medicinal product	I/25	I	20.02.03	10.03.03
Change(s) to shelf-life or storage conditions	II/27	II	24.07.03	08.10.03
Extension of Indication	II/28	II	22.10.03	27.01.04
Extension of Indication	II/29	II	22.10.03	27.01.04
Update of Summary of Product Characteristics and Package Leaflet	II/30	II	25.09.03	27.01.04
Update of Summary of Product Characteristics and Package Leaflet	II/31	II	25.09.03	27.01.04
Change in test procedure of active substance	I/32	I	22.08.03	22.09.03

[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.