Steps taken after granting the Marketing Authorisation

For procedures finalised after 1 October 2003 please refer to module 8B.

- On 14 July 1999, Janssen-Cilag International NV submitted a Type I variation, as a fulfilment of a pharmaceutical commitment, to change the specifications of the medicinal product. The Notification was signed on 28 July 1999.

- On 28 January 2000, Janssen-Cilag International NV submitted a Type I variation to introduce a change in the manufacturing process of the medicinal product. This Type I variation followed a Type II procedure and started on 18 February 2000. On 11 April 2000, the CPMP issued a positive Opinion for this variation.

- On 13 March 2000, Janssen-Cilag International NV submitted a Type I variation to extend the shelf-life of the active substance. The notification was signed on 5 April 2000.

- On 3 November 2000, Janssen-Cilag International NV submitted a Type II variation to demonstrate compliance with Commission Decision 1999/82/EC and the Note for Guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via medicinal products. On 25 January 2001, the CPMP issued a positive Opinion.

- On 30 March 2001, Janssen-Cilag Internaional NV submitted a type II variation to update part II of the dossier, namely to update the test methods for active ingredient intermediate, for active ingredient and for finished product. On 27 June 2001, the CPMP issued a positive Opinion.

- On 17 December 2001, the MAH submitted a Type I variation to extend the shelf-life of the active substance. The notification was signed on 15 February 2002.

- On 13 February 2002, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95, as amended. The Marketing Authorisation Holder applied for a variation to include the term hypertrophic granulation in the SPC and Package Leaflet following assessment of the fourth PSUR and to update the ATC code. The CPMP during its April 2002 plenary meeting considered the variation acceptable and issued on 25 April 2002 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 22 August 2002.

- On 5 July 2002, Janssen-Cilag International NV submitted a Type I variation to change the in-process controls aplied during the manufacture of the product. The notification was signed on 16 August 2002.

- On 5 July 2002, Janssen-Cilag International NV submitted a Type I variation for a change in specification of the medicinal product. The notification was signed on 16 August 2002.

- On 5 July 2002, Janssen-Cilag International NV submitted a Type I variation to change the qualitative composition of immediate packaging material. The notification was signed on 16 August 2002.

- On 31 January February 2003, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95, as amended. The variation application related to changes to the test methods and/or specifications for the finished product. The CPMP during its April 2003 plenary meeting considered the variation acceptable and issued on 25 April 2003 a positive Opinion on the Type II variation.

- On 10 June 2003 the Marketing Authorisation Holder submitted a notification pursuant to Article 61(3) of Council Directive 2001/83/EC. This change concerned an update to the contact details of the local representatives and a sentence in the Italian Package Leaflet in the section “What is Regranex”, which was moved to be in line with the English text. The MAH received a positive notification from the EMEA on 4 July 2003.

- On 1 July 2003, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95, as amended.

The variation application related to changes to the pharmaceutical documentation (update of module 3). The CPMP during its September 2003 plenary meeting considered the variation acceptable and issued on 25 September 2003 a positive Opinion on the Type II variation.