STEPS TAKEN AFTER GRANTING THE MARKETING AUTHORISATION

For procedures finalised after 1 April 2001 please refer to module 8B.

- On 16 September 1998, the European Commission authorised changes to an aspect of the labelling not connected to the SPC for Mirapexin, In accordance with Article 10(3) of Council Directive No. 92/27/EEC of 31 March 1992. The changes concerned the wording of "Expiry date" and "Batch number" in the labelling. In addition, the list of local representatives in the PL was updated.
- On 29 December 1998, the MAH submitted a line-extension application in accordance with Article 2(1) of Commission Regulation (EC) No 542/95 of March 1995, as amended, and Annex II thereof for a new 0.35 mg strength of pramipexole. On 20 May 1999 the CPMP adopted a positive opinion on the application. Following the Urgent Safety Restriction (USR) procedure for the already authorised strengths finalised on 15 July 1999, a revised opinion for the 0.35 mg strength was adopted by the CPMP on 29 July 1999 to include SPC and PL changes on sudden onset of sleep. The respective Commission Decision to authorise the 0.35 mg strength was issued on 26 October 1999.
- On 25 June 1999, the MAH provided the EMEA with new information relating to sudden onset of sleep associated with pramipexole administration. This information related to a total of 19 cases of sudden onset of sleep reported in the US. Fourteen of these occurred while patients were driving resulting in 9 car accidents with minor injuries in some cases. The MAH requested on 14 July 1999 provisional changes to prescribing and patient information through a rapid procedure. Warnings were introduced into sections 4.4, 4.5, 4.7 and 4.8 of the SPC through an USR procedure, which was finalised on 15 July 1999. The PL was amended accordingly. The MAH sent out a "Dear Doctor letter" to health professionals.
- On 7 July 1999, the MAH requested from the European Commission cancellation of the Marketing Authorisations for the 0.88 mg strengths of Mirapexin. The Commission authorised the withdrawal of this strength on 1 October 1999.
- In follow up to the USR, the MAH submitted a Type II variation in accordance with European Commission regulation (EC) No 542/95 on 23 July 1999. The MAH proposed also some minor format changes to SPC and PL. An oral clarification with the company took place on 29 July 1999 to address the quality and nature of the episodes of sudden onset of sleep and the adequacy of the proposed amendments to the product information. Following the hearing, the MAH proposed to further strengthen the wording of the warnings and CPMP adopted a positive opinion on the application on 29 July 1999. The respective Commission Decision was issued on 29 November 1999.
- On 29 February 2000 the MAH submitted an application for a Type II variation in accordance with Article 6 of European Commission regulation (EC) No 542/95. The MAH applied for an update of the SPC based on the data presented in the third Periodic Safety Update Report. The applicant proposed to include information regarding discontinuation of pramipexole treatment and requested the addition of reference to the 0.35 mg strength into the SPC. Some minor typographical corrections in the SPC and PL were also applied for. On 29 June 2000 the CPMP agreed on the wording to be implemented in the SPC and adopted a positive opinion on the Type II variation. The respective Commission Decision was issued on 20 October 2000.
- On 26 May 2000 the MAH submitted to the EMEA an application for a Type I variation in accordance with Article 4 of European Commission Regulation (EC) No. 542/95, as amended. The scope of this variation was to extend the shelf life from 2 years to 3 years. The procedure started on 30 May 2000. The EMEA notified the European Commission on 16 June 2000 that the variation was accepted. Amendments to the Annex I was required and the Commission Decision was issued on 27 July 2000.

- On 20 February 2001 the MAH submitted to the EMEA an application for a Type I variation in accordance with Article 4 of European Commission Regulation (EC) No. 542/95, as amended. The scope of this variation was to replace an excipient. The procedure started on 1 March 2001. The EMEA notified the European Commission on 30 March 2001 that that the variation was accepted and did not require any amendments to the Community Marketing Authorisation.