Steps taken after granting the Marketing Authorisation

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

- On 15 January 2001, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95. The Marketing Authorisation Holder applied for an extension of the therapeutic indication to include Chronic Idiopathic Urticaria. The CPMP during its April 2001 plenary meeting considered the variation acceptable and issued on 25 April 2001 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 6 August 2001.
- On 15 January 2001, the Marketing Authorisation Holder submitted an application for a Type II variation in accordance with Art. 6 of Commission Regulation (EC) No. 542/95. The Marketing Authorisation Holder applied for an update of the SPC to include new information on interactions. The CPMP during its May 2001 plenary meeting considered the variation acceptable and issued on 31 May 2001 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 20 September 2001.
- On 22 January 2002, the Marketing Autorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) 542/95, as amended. The MAH applied for an additional manufacturing site. The EMEA considered this variation to be acceptable and issued on 26 February 2002 a positive Notification for the Type I variation application.
- On 3 August 2001, 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 an update of the SPC to include new information on interactions. The CPMP during its December 2001 plenary meeting considered the variation acceptable and issued on 13 December 2001 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 12 April 2002.
- On 12 January 2001, the Marketing Authorisation Holder submitted an application for Neoclarityn 0.5 mg/ml syrup pursuant to Article 2(1) of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended, and Annex II point 3 (iv). The CPMP during its December 2001 plenary meeting considered the application acceptable and issued on 13 December 2001 a positive Opinion for granting a Marketing Authorisation for Neoclarityn 0.5 mg/ml syrup. The corresponding Commission Decision was issued on 16 April 2002.
- On 9 March 2001, the Marketing Authorisation Holder submitted an application for Neoclarityn 5 mg oral lyophilisate pursuant to Article 2(1) of Commission Regulation (EC) No 542/95 of 10 March 1995, as amended, and Annex II point 3 (iv). The CPMP during its December 2001 plenary meeting considered the application acceptable and issued on 13 December 2001 a positive Opinion for granting a Marketing Authorisation for Neoclarityn 5 mg oral lyophilisate. The corresponding Commission Decision was issued on 16 April 2002.
- On 3 August 2001, the Marketing Authorisation Holder submitted an application for a Type II variation for the Neoclarityn 5 mg tablets in accordance with Art. 6 of Commission Regulation (EC) No. 542/95 as amended. The Marketing Authorisation Holder applied for an extension for Neoclarityn 5 mg film-coated tablets of the therapeutic indication from seasonal allergic rhinitis to allergic rhinitis. The CPMP during its February 2002 plenary meeting considered the variation acceptable and issued on 21 February 2002 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 17 May 2002.
- On 15 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 for Neoclarityn 5 mg film-coated tablets, Neoclarityn 0.5 mg/ml syrup and Neoclarityn 5 mg oral lyophilisate. The Marketing Authorisation Holder applied for a variation to include the term hypersensitivity in the SPC and Package Leaflet following assessment of the first PSUR. 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 18 July 2002.

- On 5 June 2002, the Marketing Autorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) 542/95, as amended. The MAH applied for an additional manufacturing site. The EMEA considered this variation to be acceptable and issued on 7 August 2002 a positive Notification for the Type I variation application.
- On 5 June 2002, the Marketing Autorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) 542/95, as amended. The MAH applied for a change of the manufacturer responsible for batch release. The EMEA considered this variation to be acceptable and issued on 7 August 2002 a positive Notification for the Type I variation application.
- On 5 June 2002, the Marketing Autorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) 542/95, as amended. The MAH applied for a change in manufacture of the medicinal product and as consequential changes the MAH applied for a change in specification of medicinal product and a change in test procedures of the medicinal product. The EMEA considered this variation to be acceptable and issued on 7 August 2002 a positive Notification for the Type I variation application.
- On 15 April 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 for for Neoclarityn 0.5 mg/ml syrup and Neoclarityn 5 mg oral lyophilisate. The Marketing Authorisation Holder applied for an extension of the therapeutic indication from seasonal allergic rhinitis to allergic rhinitis. The CPMP during its June 2002 plenary meeting considered the variation acceptable and issued on 27 June 2002 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 30 September 2002.
- On 15 April 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 for for Neoclarityn 0.5 mg/ml syrup and Neoclarityn 5 mg oral lyophilisate. The Marketing Authorisation Holder applied for an update of the SPC to include new information on interactions. The CPMP during its June 2002 plenary meeting considered the variation acceptable and issued on 27 June 2002 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 30 September 2002.
- On 12 February 2003, the Marketing Authorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) 542/95, as amended. The MAH applied for an addition of manufacturing site for manufacturing, primary and secondary packaging. The EMEA considered this variation to be acceptable and issued on 17 March 2003 a positive Notification for the Type I variation application.
- On 12 February 2003, the Marketing Authorisation Holder submitted an application for a Type I variation in accordance with Commission Regulation (EC) 542/95, as amended. The MAH applied for minor changes in the manufacture of the medicinal product. The EMEA considered this variation to be acceptable and issued on 17 March 2003 a positive Notification for the Type I variation application.
- On 25 April 2002, Sweden triggered a referral to the EMEA under Article 31 of Directive 2001/83/EC, based on the data from the Swedish Medical Birth Registry, which could not exclude that the use of loratadine during the first trimester of pregnancy may be associated with increased risk of hypospadias. As desloratadine is the major metabolite of loratadine, any safety or efficacy issues emerging for loratadine might be relevant also for desloratadine and a referral was therefore also triggered for desloratadine containing medicinal products. Following consultation with the Commission, it was decided to introduce the conclusion of CPMP's scientific assessment via a Type II variation.

The CPMP concluded the scientific assessment of the data submitted in the context of the safety issue on hypospadia following use of desloratadine during pregnancy including recommendations for changes to the Summary of Product Characteristics.

The MAH was requested to submit a Type II variation to implement the changes to the SPC and Package Leaflet as requested in the conclusion of the scientific assessment.

On 5 December 2002, the Marketing Authorisation Holder therefore 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 change to section 4.6 of the SPC to state that the safe use of the drug during pregnancy has not been established and that the use of desloratadine during pregnancy is therefore not recommended. The CPMP during its December 2002 plenary meeting considered the variation acceptable and issued on 18 December 2002 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 17 March 2003.

- On 14 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 for Neoclarityn. The Marketing Authorisation Holder applied to include in the SPC and the Package Leaflet the following terms: 'elevated liver enzymes', 'increased bilirubin', 'tachycardia', and 'palpitations' and to specifically mention angioedema, pruritus and urticaria in the statement on hypersensitivity. 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. The corresponding Commission Decision was issued on 30 July 2003.
- On 14 March 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 for Neoclarityn. The Marketing Authorisation Holder applied to include in the SPC and the Package Leaflet the following terms: 'diarrhoea', 'abdominal pain', 'dyspepsia', 'nausea', and 'vomiting' and to reorganise section 4.8 of the SPC according to system organ class. 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. The corresponding Commission Decision was issued on 30 July 2003.
- On 18 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 for Neoclarityn. The Marketing Authorisation Holder applied to include in section 4.8 of the SPC the following terms: 'somnolence' and 'dizziness' and subsequent changes to section 4.7 and 5.1 of the SPC. These changes were also reflected in the Package Leaflet. The CPMP during its November 2003 plenary meeting considered the variation acceptable and issued on 20 November 2003 a positive Opinion on the Type II variation. The corresponding Commission Decision was issued on 12 February 2004.
- The MAH submitted on 15 April 2004 a request to introduce changes to an aspect of the Package Leaflet not connected to the SPC, in accordance with Article 61(3) of Council Directive No 2001/83/EC, as amended. The Marketing Authorisation Holder applied for the inclusion of additional local representatives of the Marketing Authorisation Holder for all new Member States. The MAH received a positive notification from the EMEA on 13 May 2004.