**BACKGROUND INFORMATION ON THE PROCEDURE**

## 1. Submission of the dossier

The applicant Encysive (UK) Limited submitted on 28 July 2005 an application for Marketing Authorisation to the European Medicines Agency (EMEA) for Thelin, through the centralised procedure falling within the Article 3(1) and point 4 of Annex of Regulation (EC) No 726/2004. The eligibility to the centralised procedure was agreed upon by the EMEA/CHMP on 25 May 2005.

The legal basis for this application refers to:

Article 8.3 of Directive 2001/83/EC, as amended - complete and independent application

The applicant Encysive (UK) Limited submitted on 28 July 2005 an application for Marketing Authorisation to the European Medicines Agency (EMEA) through the centralised procedure for Thelin, which was designated as an orphan medicinal product EU/3/04/234 on 21 October 2004. Thelin was designated as an orphan medicinal product in the following indication: Treatment of pulmonary arterial hypertension and chronic thromboembolic pulmonary. The calculated prevalence of this condition was below 2 per 100,000 EU population.

The applicant applied for the following indication "for the treatment of pulmonary arterial hypertension in patients with WHO Class II, III, or IV symptoms to improve exercise ability, functional status, and decrease the rate of clinical worsening."

**Information relating to Orphan Market Exclusivity**

**Similarity**
Pursuant to Article 8 of Regulation (EC) No. 141/2000 and Article 3 of Commission Regulation (EC) No 847/2000, the application contained a critical report addressing the possible similarity with authorised orphan medicinal products (see Appendix 1).

**Scientific Advice**
The applicant did not seek scientific advice or Protocol Assistance at the CHMP.

**Licensing status:**
The product was not licensed in any country at the time of submission of the application.

The Rapporteur and Co-Rapporteur appointed by the CHMP and the evaluation teams were:

| Rapporteur: | Co-Rapporteur: |
|---|---|
| Dr. J.F.F. Eckherkerker | Dr. K. Broich |

EMEA Product Team Leader: A. Zanoletty

## 2. Steps taken for the assessment of the product

- The application was received by the EMEA on 28 July 2005.
- The procedure started on 17 August 2005.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 28 October 2005 (Annex 1). The Co-Rapporteur's first Assessment Report was circulated to all CHMP members on 04 November 2005 (Annex 2).
- During the meeting on 12 –15 December 2005, the CHMP agreed on the consolidated List of Questions to be sent to the applicant. The final consolidated List of Questions was sent to the applicant on 15 December 2005 (Annex 3).
- The applicant submitted the responses to the CHMP consolidated List of Questions on 17 February 2006.
- The summary report of the inspection carried out at the following site(s) Aptuit, Inc 10245 Hickman Mills Drive, Kansas City, Missouri 64134-0708, between 18-20 April 2006 was issued on 12 May 2006.
- The Rapporteurs circulated the Joint Assessment Report on the applicant's responses to the List of Questions to all CHMP members on 21 April 2006 (Annex 4).
- During the CHMP meeting on 24-27 April 2006, the CHMP agreed on a list of outstanding issues to be addressed in writing by the applicant. The final consolidated List of Outstanding issues was sent to the applicant on 27 April 2006. (Annex 5).
- The applicant submitted the responses to the CHMP list of outstanding issues on 10 May 2006.
- The Rapporteurs circulated a Joint Assessment Report on the applicant's responses to the List of outstanding issues to all CHMP members on 19 May 2006 (Annex 6).
- During the meeting on 29 May –1 June 2006, the CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a Marketing Authorisation to Thelin on 1 June 2006. The applicant provided the letter of undertaking on the follow-up measures to be fulfilled post-authorisation on 30 May 2006 Annex 7.
- The CHMP adopted a report on similarity of Thelin with Tracleer (bosentan), Ventavis (iloprost) on 14 – 17 November, and with Revatio (sildenafil) on the 1 June 2006. (see Appendix 5.1.)
- The CHMP opinions were forwarded, in all official languages of the European Union, to the European Commission, which adopted the corresponding Decisions on 10 August 2006.