Procedural steps taken and scientific information after the authorisation
Changes made after 01/09/2003

Zerene

For procedures finalised before 01/09/2003, please refer to module 8A

MAJOR CHANGES[1]

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
R/0022	Renewal of the marketing authorisation			SPC, Annex II, Labelling, PL	Based on their review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP was of the opinion that the quality, safety and efficacy continue to be adequately and sufficiently demonstrated. Therefore, the benefit/risk profile of Zerene continues to be favourable. The Marketing Authorisation for Zerene is renewed with unlimited validity.
T/0021	Transfer of Marketing Authorisation Holder	13/12/2007	18/01/2008	SPC, Labelling, PL	
II/0018	Update of the section 4.4 (Special warnings and precautions for use) of the Summary of Product Characteristics (SPC) to include warnings regarding complex sleep-related behaviours and anaphylactic/anaphylactoid reactions (specifically angioedema). Additionally, section 4.8 (Undesirable effects) of the SPC and relevant sections of the Package Leaflet (PL) have been updated accordingly. Furthermore, changes to the labelling and Package Leaflet have been introduced, in accordance with the QRD template and the contact details for the local representative of Bulgaria and Romania has been included.	18/10/2007	21/11/2007	SPC, Labelling, PL	The MAH performed a cumulative review of the post-marketing safety surveillance database up to March 2007. In this review, 12 reports suggestive of complex sleep behaviour were identified. They include cases of sleep-walking, sleep-driving and other complex behaviours such as preparing and eating food. On the basis of this review, the MAH proposed to include a warning in section 4.4 of the SPC. Furthermore, due to the risk to the patients in the community, it is also recommended that zaleplon should be discontinued for patients who report sleep-driving episodes. From the cumulative review, 8 reports of angioedema were also identified. On this basis, the MAH proposed a warning to inform that cases of anaphylactic/anaphylactoid reactions (specifically angioedema) have been reported. The MAH also proposed to update section 4.8 of the SPC (Undesirable

[1] Major changes e.g. Type II variations, Annex II applications, Renewals and Annual Reassessments
[2] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet)

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					effects) to add sleep-walking and angioedema. Section 2 (Before you take Zerene) and section 4 (Possible side-effects) of the PL have also been updated to reflect the above SPC changes. Additionally, the MAH is proposing to update the PL in accordance with QRD Template version 7.2, and to update the address list of local representatives in section 6 (Further Information) with the inclusion of contact details for representatives in Bulgaria and Romania.
II/0017	Update of Summary of Product Characteristics (section 4.4 Special Warnings and Special Precautions for Use) to include a specific warning on the potential for dependence with zaleplon. Corresponding changes have been introduced in section 2 of the Package Leaflet.	27/04/2006	12/06/2006	SPC, Annex II, Labelling, PL	In the 9th Periodic Safety Update Report (PSUR) for Zerene, 4 case reports of dependence were included. In view of this the CHMP requested the MAH to update the Product Information accordingly. Subsequently, the MAH identified in its database 14 reports consistent with dependence on zaleplon. Most of the patients were taking other psychotropic medications. Therefore, the following information has been included in the Summary of Product Characteristics: "There have been post-marketing reports of dependence associated with zaleplon predominantly in combination with other psychotropic agents." The Package Leaflet was updated accordingly. In addition, in this Type II variation, the MAH updated the list of local representatives and updated the Product Information in accordance to the latest template.
II/0016	Update of sections 4.8 and 4.9 of the SPC and consequent changes of the PL following CHMP assessment of the PSUR 8.	26/05/2005	04/07/2005	SPC, PL	Section 4.8 (Undesirable effects) of the SPC was updated to reflect the available info on hepatotoxicity (mostly described as increased transaminase levels). In section 4.9 (Overdose), information was added that chromaturia (blue-green urine discolouration) has been reported in connection with zaleplon overdose.
R/0014	Renewal of the marketing authorisation	21/01/2004	31/03/2004	SPC, Annex II, Labelling, PL	The CHMP was of the opinion that the quality, safety and efficacy of Zerene continues to be adequately demonstrated and therefore that the benefit/risk profile of Zerene remains favourable in the approved indication.

MINOR CHANGES[3]

No	Scope	Product Information affected[2]	Date[4]
IA/0023	07_b_01_Replacement/add. of manufacturing site: Primary packaging site - Solid forms 08_b_02_Change in BR/QC testing - repl./add. manuf. responsible for BR - incl. BC/testing	Annex II, PL	23/06/2009
IA/0020	04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)		13/09/2007
IA/0019	04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.) 05_Change in the name and/or address of a manufacturer of the finished product		10/09/2007
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	PL	09/06/2004
IA/0013	22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer		20/10/2003

[3] Minor changes e.g. Type I variations and Notifications
[4] Date of entry into force of the change