DULOXETINE BOEHRINGER INGELHEIM

Procedural steps taken and scientific information after the authorisation

MAJOR CHANGES[1]

No	Scope	Opinion issued on	Commission Decision Issued/ amended on	Product Information affected[2]	Summary
II/0011	Update of the Detailed Description of Pharmacovigilance System (DDPS) in the Annex II, including formal notification of a change in the administrative data of the marketing authorisation application form.	23/07/2009	17/09/2009	Annex II	The Detailed Description of the Pharmacovigilance System has been updated (Version 5.2 dated April 2009) to notify changes performed since the last approved version. Consequently, Annex II has been updated with the new version number and date of the agreed DDPS.
II/0008	Update of section 4.5 of the Summary of Product Characteristics to reflect the results of a recent duloxetine/warfarin interaction study (study F1J-MC-HMFP). Furthermore, the term "adolescents" was included in section 4.2 of the SPC in order to align this section with the current QRD template.	29/05/2009	14/07/2009	SPC	Study F1J-MC-HMFP was an open-label study with the primary objective to evaluate the anticoagulant effects of multiple doses of warfarin when taken at the same time with multiple doses of duloxetine as measured by changes in the international normalized ratio (INR). Increases in INR values were reported when duloxetine was co-administered with warfarin. However, concomitant administration of duloxetine with warfarin under steady state conditions, in healthy volunteers, as part of a clinical pharmacology study, did not result in a clinically significant change in INR from baseline or in the pharmacokinetics of warfarin.
II/0007	Quality changes to change the finished product specification.	23/04/2009	28/04/2009		
II/0002	Update of Sections 4.8 "Undesirable effects" and 4.9 "Overdose" of the Summary of Product Characteristics (SPC) to reflect the most recent clinical trial data findings of the 7th PSUR. The Package Leaftlet (PL) was updated accordingly.	19/02/2009	03/04/2009	SPC, PL	A new data lock point for all placebo-controlled clinical studies resulted in a significant increase in the size of the overall database and thus a more robust basis for the determination of Adverse Drug Reactions (ADRs). As a consequence, the frequency of some ADRs was updated in the SPC. Regarding spontaneous data, the MAH identified one new ADR

[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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	In addition, this variation implements the outcome of a recent user testing of the PL of duloxetine-containing products.				("restless legs syndrome") as well as new information on overdose in the most recent PSUR (PSUR 7) submitted in September 2008, and updated the SPC accordingly. Finally, the MAH has undertaken a user testing of the PL of duloxetine-containing products and the results of these were implemented in the PL.
II/0001	Update of sections 4.2 and 5.1 of the Summary of Product Characteristics to reflect new data from a clinical study that investigated the maintenance of effect of duloxetine over 6 months of treatment. The opportunity is also taken to correct some minor typos in the SPC, Labelling and Package Leaflet.	22/01/2009	10/03/2009	SPC, Labelling, PL	Study 'HMEM' was designed to investigate the maintenance of effect of duloxetine 60 mg once daily in patients with Diabetic Peripheral Neuropathic Pain (DPNP) who responded to an initial 8 weeks of therapy. This variation application was submitted in order to update the SPC to reflect the results of study HMEM. The study demonstrated that, for patients who showed an initial response to DPNP therapy with duloxetine, the pain relief observed with duloxetine 60 mg is maintained over a 6-month period. The variation resulted in the following SPC wording: Section 4.2: [Diabetic Peripheral Neuropathic Pain Response to treatment should be evaluated after 2 months. In patients with inadequate initial response, additional response after this time is unlikely…] Section 5.1 […In an open label long-term uncontrolled study, the pain reduction in patients responding to 8-weeks of acute treatment of DULOXETINE BOEHRINGER INGELHEIM 60 mg once daily was maintained for a further 6-months as measured by change on the Brief Pain Inventory (BPI) 24-hour average pain item…]

MINOR CHANGES[3]

No	Scope	Product Information affected[2]	Date[4]
IA/0015	47_b_Deletion of a strength	SPC, Labelling, PL	07/12/2009
IA/0014	22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer To submit new, updated and unchanged TSE Ph. Eur. certificates of suitability for the gelatine used by the current authorised manufacturer of the capsules and for an alternative new suppplier.		24/11/2009
IB/0013	35_b_Change in weight of coating/capsule shells - gastro-res., modif., prol. release ph. forms		24/11/2009
IB/0012	34_b_01_Change in colour/flavour - Increase or addition: colouring system		13/11/2009
IB/0009	07_c_Replacement/add. of manufacturing site: All other manufacturing operations ex. batch release		27/04/2009
IA/0010	32_b_Change in batch size of the finished product - downscaling down to 10-fold		02/04/2009
IA/0006	38_a_Change in test procedure of finished product - minor change to approved test procedure		24/02/2009
IB/0004	33_Minor change in the manufacture of the finished product		15/01/2009
IB/0003	13_b_Change in test proc. for active substance - other changes (replacement/addition)		15/01/2009

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