


Medicines Evaluation Board

Dear 

Please consider this as AstraZeneca's response to the Pharmacovigilance Working Party's request to include the following adverse events to Sections 4.4 and 4.8 of the Summary of Product Characteristics for statins as a class:

- Sleep disturbance (including insomnia) and parasomnia
- Memory loss
- Sexual disturbance
- Depression
- Interstitial lung disease

AstraZeneca Response

As requested by the MEB in March of 2006, AstraZeneca completed and submitted a review of six topics: sleep disturbance, memory loss, micturition disorders, sexual dysfunction, depression, and interstitial pneumopathy. At that time, following a cumulative review of clinical trial data, spontaneous post-marketing safety data, and literature, a causal relationship with CRESTOR and the aforementioned events was not established. Since then, all topics have been kept under close surveillance. Additionally, both periodic and/or cumulative reviews for all events except interstitial lung disease were presented in one or more of the Periodic Safety Update Reports in the list that follows. The adverse event of memory loss was added to the AstraZeneca Core Data Sheet Section 4.8 Undesirable Effects, Post-Marketing Experience on 29 November 2006 and subsequently the Summary of Product Characteristics.

- **Sleep disturbance (including insomnia) and parasomnia**
 - Cumulative review PSUR #8 (07 May 2006 through 06 November 2006)
 - Periodic review PSUR #9 (07 November 2006 through 06 May 2007)
 - Periodic review PSUR #10 (07 May 2007 through 06 November 2007)
- **Memory loss**
 - Cumulative review PSUR #8 (07 May 2006 through 06 November 2006)
 - Memory loss was added to the AstraZeneca Core Data Sheet on 29 November 2006
 - Periodic review PSUR #9 (07 November 2006 through 06 May 2007)

- **Sexual disturbance**
 - Cumulative review PSUR #8 (07 May 2006 through 06 November 2006)
 - Periodic review PSUR #9 (07 November 2006 through 06 May 2007)
 - Periodic review PSUR #10 (07 May 2007 through 06 November 2007)

- **Depression**
 - Cumulative review PSUR #8 (07 May 2006 through 06 November 2006)
 - Periodic review PSUR #9 (07 November 2006 through 06 May 2007)
 - Cumulative review PSUR #10 (07 May 2007 through 06 November 2007)

- **Interstitial lung disease**
 - Cumulative review as requested by the Pharmacovigilance Working Party; March 2006

AstraZeneca Conclusion

Based on the totality of data including review of clinical trial, spontaneous post-marketing safety data, and literature, AstraZeneca has not established a causal association with the events of sleep disturbance, sexual dysfunction, depression, and interstitial lung disease and CRESTOR. AstraZeneca continues to keep these events under close surveillance. No changes to the Core Data Sheet or Summary of Product Characteristics are warranted at this time.

If there are any data available from the Pharmacovigilance Working Party with respect to CRESTOR and its association to these adverse events, then AstraZeneca would be pleased to review this evidence as we do not agree with the statin class labelling and the addition of these events to the CRESTOR SmPC as suggested.

On behalf of AstraZeneca Patient Safety,

████████████████████
████████████████████
████████████████████ - CRESTOR
AstraZeneca LP
FOC-NW2-065
Wilmington, DE
████████████████████