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Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Active substance(s): bimatoprost / timolol

Procedure No. EMEA/H/C/PSUSA/00002961/201511

Period covered by the PSUR: 20 November 2012 – 19 November 2015

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Scientific conclusions and grounds for variation to the terms of the marketing authorisations

In the current PSUR, a large number of cases include immediate local ocular tissue irritation, angioedema, urticarial, eczema and allergic dermatitis. Furthermore, some of these included positive rechallenge and dechallenge. It is noted that hypersensitivity is a listed ADR in the timolol Product Information. Therefore, the PRAC agreed that 'Hypersensitivity reaction including signs and symptoms of allergic dermatitis, angioedema, eye allergy' should be added in section 4.8 for both Ganfort and Ganfort PF.

14 cases of nightmare were reviewed in the current PSUR, which included cases of both positive dechallenge and rechallenge. 14 cases of insomnia were reviewed and these also included positive dechallenge experience. Nightmare and insomnia are listed as an ADR in the timolol Product Information. Therefore, the PRAC agreed that 'Nightmare and Insomnia' should be added in section 4.8 for Ganfort.

Dysgeusia was evaluated in a review of 12 cases (one serious and 11 non-serious cases). In the cases evaluated close temporal relationship was reported coupled with a possible mode of action which supports a causal relationship between Ganfort and Dysgeusia. Therefore, the PRAC agreed that 'Dysgeusia' should be added in section 4.8 for Ganfort.

Eye swelling was evaluated in a review of 30 cases. A close temporal relationship was reported and also positive dechallenge experience which support a causal relationship between Ganfort / Ganfort PF and Eye swelling. Therefore, the PRAC agreed that 'Eye swelling' should be added in section 4.8 for both Ganfort and Ganfort PF.

A review of 46 cases with blurred vision, some with close temporal relationship and positive dechallenge support a causal relationship between Ganfort and Vision blurred. Furthermore, Vision blurred is listed as an additional ADR associated with the timolol component of Ganfort in the CCDS. Therefore, the PRAC agreed that 'Vision blurred' should be added in section 4.8 for Ganfort.

Bradycardia was evaluated as a potential safety signal and 15 cases were reviewed. These showed a close temporal relationship and positive rechallenge and dechallenge which support a causal relationship between Ganfort / Ganfort PF and bradycardia. Bradycardia is also a well-known pharmacological effect from systemic beta blocker treatment. Therefore, the PRAC agreed that 'Bradycardia' should be added in section 4.8 for both Ganfort and Ganfort PF.

Alopecia was evaluated as a potential safety signal with 23 cases which included close temporal relationship and positive dechallenge and rechallenge experience which support a causal relationship between Ganfort and Alopecia. Therefore, the PRAC agreed that 'Alopecia' should be added in section 4.8 for Ganfort.

In a safety review of 26 cases of Fatigue, a close temporal relationship and positive dechallenge and rechallenge experience was reported which support a causal relationship between Ganfort and Fatigue. Therefore, the PRAC agreed that 'Fatigue' should be added in section 4.8 for Ganfort.

Asthma is currently a listed ADR in the timolol Product Information. Asthma and asthma-related symptoms cases were evaluated in the present PSUR. It showed a close temporal relationship and positive rechallenge and dechallenge which support a causal relationship Ganfort PF and Asthma and other asthma-related symptoms including dyspnea and wheezing. Therefore, the PRAC agreed that that 'Asthma' should be added in section 4.8 for Ganfort and Ganfort PF and 'Dyspnoea' in section 4.8 for Ganfort PF.

Therefore, in view of the data presented in the reviewed PSUR, the PRAC considered that changes to the product information of medicinal products containing bimatoprost/timolol were warranted.