2.7 Clinical Summary

2.7.1 Overview of the Clinical Testing Strategy

The formulation of bimatoprost/timolol manufactured by Pharmathen S.A. refers to the drug product combination of bimatoprost 0.3 mg/mL and timolol 5.0 mg/mL preservative free, eye drops solution in multidose container.

The present marketing authorisation application is related to a medicinal product claiming essential similarity to Ganfort preservative free eye drops solution in single dose container (Allergan) and authorised pursuant to Article 10(3) hybrid application of Directive 2001/83/EC.

As no new additional studies have been provided within the documentation, a full Clinical Summary is not included.

According to the Guideline on the Investigation of Bioequivalence (CPMP/QWP/EWP/1401/98 Rev. 1, Corr*):

A waiver of the need to provide equivalence data may be acceptable in the case of solutions, e.g. eye drops, nasal sprays or cutaneous solutions, if the test product is of the same type of solution (aqueous or oily), and contains the same concentration of the same active substance as the medicinal product currently approved. Minor differences in the excipient composition may be acceptable if the relevant pharmaceutical properties of the test product and reference product are identical or essentially similar. Any qualitative or quantitative differences in excipients must be satisfactorily justified in relation to their influence on therapeutic equivalence.

Bimatoprost/timolol preservative-free eye drops by Pharmathen is available in a multiple dose container. It contains the same active substances, bimatoprost and timolol, with the same excipient composition to Ganfort eye drops solution in single dose container authorised in the in the Community based on the basis of a complete dossier in accordance with the provisions set forth in Article 8 and 10 of Directive 2001/83/EC, as amended.

The Pharmathen product is quantitatively the same to Ganfort in terms of concentration of bimatoprost and timolol maleate. In Ganfort, the concentrations of sodium phosphate dibasic heptahydrate and citric acid monohydrate (buffers), which

are used to adjust the pH of the solution to 7.3, and sodium chloride (tonicity agent), which is used to adjust tonicity to 290 mOsm/kg, were not quantified. By selecting the appropriate concentrations of these three salts, the applicant's product displays similar osmolality to Ganfort eye drops solution in single dose container, and has a similar and stable pH throughout stability testing (shelf life). HCl or NaOH solution is used for final pH tuning, if necessary. Any potential quantitative differences are minor due to the stable and similar final pharmaceutical product characteristics of the two formulations. As all pharmaceutical properties of the applicant's product are similar to those of reference product, the therapeutic equivalence of the products is assured.

Since the product under consideration is an aqueous solution, is qualitatively and quantitatively similar to the reference product for active ingredients and excipients, and displays similar physiochemical properties, a waiver of the need to provide equivalence data is requested.

The majority of the clinical data appearing in the overview are based solely on bibliographical research. The cited articles refer to reviews and/or clinical studies performed in humans.