2.7 Clinical Summary

The generic formulation of travoprost manufactured by Pharmathen S.A. refers to the drug product Travoprost/Pharmathen 40 µg/mL preservative free eye drops, solution in multi dose container, which is indicated for the decrease of elevated intraocular pressure in adult patients with ocular hypertension or open-angle glaucoma.

The present marketing authorisation application is related to a generic medicinal product claiming essential similarity to Travatan® (travoprost) eye drops solution 40 µg/mL (Alcon Laboratories, Inc.) and authorised pursuant to Article 10(3) hybrid application of Directive 2001/83/EC.

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

As Travoprost is not new chemical entity, and this application is for a generic product claiming essential similarity to Travatan (Alcon Laboratories Limited), and as no new additional studies has 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.*

Except for the exclusion of the preservative in the applicant's formulation, its product is essentially similar to the originator product in formulation and dosage form. The physicochemical properties and the ingredients of both products (both active and non-active) are essentially similar (see *Section 3.2.P.2.2*). Specifically:

1. Surface tension is known to play an important role in the bioavailability of the drug substance in eye drops. To ensure pharmaceutical equivalence between the test and reference products, comparative surface tension data are provided. The method used to measure surface tension and the results of the tests are described in *Section 3.2.P.2.2.* The data demonstrates that all three pilot batches have similar surface tension values to those of the originator's products available on the European market. Therefore, surface tension issues are considered resolved from a physicochemical point of view.

2. An extensive *in vitro* investigation of the product was performed and compared to Travatan from several different European markets. Analysis of surface tension, average deliverable volume/variation and total number of drops per container results are presented, as well as appearance, Assay, Related substances, pH, specific gravity and osmolality results. These comparative *in vitro* data are presented in *Section 3.2.P.2.2.* On reviewing all results of the generic product batches versus the originators, it can be concluded that physicochemical characteristics are similar.

A justification for claiming a waiver from conducting *in vivo* clinical studies was provided during a Scientific Advice procedure with the Danish Health and Medicines Authority (full justification can be found in Module 2.5 section 2.5.3.1.: Biowaiver). This justification was accepted by the DHMA.

It was argued that *in vivo* data was not required in conformance with Guideline CPMP/EWP/239/95 and Guideline on the Investigation of Bioequivalence (CPMP/QWP/EWP/1401/98 Rev. 1, Corr*) as Travoprost/Pharmathen 40 µg/mL preservative free eye drops, solution in multi dose container is an ophthalmic solution and its composition is essentially to the composition of the originator product.

In conclusion, the quality data demonstrates that the proposed product is essentially similar to the originator product in formulation and dosage form. Significantly, the physicochemical properties of both products are essentially similar. Therefore, Travoprost/Pharmathen 40 µg/mL preservative free eye drops, solution in multi dose container poses no potential risk to public health and safety.