Acanthamoeba keratitis (AK) is a rare but severe infectious disease caused by Acanthamoeba spp., a ubiquitous free-living protozoan. The incidence is uncertain but probably <500 cases/year based on the EU population of about 500 million, and as low as 0.15-0.18 per million in the USA (Acharya et al., 2007). In the absence of treatment, the disease progresses to blindness as a result of corneal vascularisation and scarring or corneal perforation. PHMB 0.02% eye drops is a unlicensed product which is empirically used to treat AK. Recently (Asero et al., IOVS 2015) it has been identified in PHMB 0.08% eye drops a potential effective drug product for treating AK. The objective of this study is to establish if PHMB 0.08% eye drops is sufficiently safe as a selected concentration to be tested in healthy human volunteers.

METHODS

In accordance with the European Medicine Agency Guideline on repeated dose toxicity CPMP/SWP/1042/99 a low dose (0.08%) of PHMB eye drops with established therapeutic effect, together with a high dose (0.8%) of PHMB, eye drops selected to enable identification of toxicity and an intermediate dose (0.25%) of PHMB eye drops, such as the geometric mean between the high and the low dose, have been selected for conducting a two-week tolerance/toxicity study in rabbit. All animal procedures were performed according to the guidelines of the ARVO statement for the ”Use of Animals in Ophthalmic and Vision Research”.

A total of 21 male and 21 female New Zealand White rabbits, approximately 8 weeks old, were distributed in four Groups with 8 animals each (4 male and 4 female rabbits) in Groups 2 and 3; 12 animals each in Groups 1 and 4 (6 male and 6 female rabbits). Rabbits were instilled into the right eye with 50 µL of PHMB vehicle (Group 1), PHMB 0.08%, 0.25% and 0.8% eye drops (Groups 2, 3 and 4), 13 times a day at approximately 1 hour intervals from Day 1 to 7 (first week) and 7 times a day at approximately 2 hours intervals from Day 8 to 14 (second week). The left eye remained untreated. Two animals per sex of Groups 1 and 4, were sacrificed after 1 week of recovery. Ocular irritation assessment was performed daily, before first dosing, in all animals during the treatment and once daily during the recovery period. In addition, fluorescein staining of cornea, slit-lamp examination and ophthalmoscopy were performed at weekly intervals in all animals during the study (Baldwin et al.). Macroscopic and microscopic examination of treated and untreated eyes were performed in all animals sacrificed at the end of the treatment.

REFERENCES