

OVERVIEW

MESOTRIONE (ZA1296)

7/18/2000

Study Type: Non-Guideline; Ocular Lesions in Rats Fed Tyrosine

Work Assignment No. 2-01-52J (amend 1) (MRID 44537105)

Prepared for

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MESOTRIONE

Ocular Lesions in Rats Fed Tyrosine (non-GDL)

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OVERVIEW

STUDY TYPE: Ocular Lesions in Rats Fed Tyrosine

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CITATION: Robinson, M., (1995) A Study to Investigate the Morphology and Pathology of Ocular Lesions in Alpk:AP_{SD} Rats Fed Different Levels of Tyrosine in a Low Protein Diet. Central Toxicology Laboratory, Cheshire, UK. Laboratory Report No.: CTL/R/1243, June 21, 1995. MRID 44537105. Unpublished.

SPONSOR: Zeneca AG Products, Wilmington, Delaware

Executive Summary: The objective of this study (MRID 44537105) was to investigate ocular lesions in rats fed tyrosine in the diet. Alpk:AP_{SD} weanling rats (21-23 days old; 8/group) were fed a low protein diet (PCD low protein diet) supplemented with 0, 0.5, 1.0, 2.5, or 5% (w/w) L-tyrosine (100% purity assumed) for 21 days. Ophthalmoscopic examinations were performed during acclimatization, daily on days 2 through 8, and on days 11, 12, 14, 18, and 21. Upon detection of corneal lesions in the majority of the rats in a group, the group was terminated. All remaining groups were terminated on day 21. All of the rats were necropsied and the eyes and Harderian glands examined by light microscopy.

Corneal lesions were first detected on day 3 in the 5.0% group (5/8 rats) and by day 4 (2/8 rats) in the 2.5% tyrosine group. By days 4 and 6, respectively, 6/8 rats in each group were affected. The lesions started as single or multiple small foci of opacity, which with time coalesced to produce larger areas of opacity. Fixation of the iris, indicating iritis, was observed in both the 2.5 and 5.0% groups (1/8 rats, each). Histopathological examination detected minimal/slight keratitis in both effected groups (4/8 rats, each); the keratitis was characterized by polymorphonuclear leucocyte infiltration of the corneal outer stroma and focal corneal epithelium disorganization. Minimal epithelial disorganization without inflammation was observed in 2/8 rats fed 5% tyrosine. The results of this special study are presented as an attachment to this overview (study report Tables 2 and 3, pages 10 and 11).

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In conclusion, tyrosine at levels of 2.5 and 5% in a low protein diet induces ocular toxicity in Alpk:AP_{SD} weanling rats.

ATTACHMENT

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