

HYDRALAZINE (Group 3)

A. Evidence for carcinogenicity to humans (*inadequate*)

Two studies suggest an association between exposure to hydralazine and cancer. One was confined to patients with and without signs of toxicity due to hydralazine, and potential confounding factors were not controlled for. The other involved a small number of subjects exposed to hydralazine, but the possibility of selection bias could not be excluded¹. However, a study of 3988 participants in a hypertensive detection and follow-up programme suggested no increased risk for cancers at all sites from use of hydralazine. A logistic regression estimate of cancer risk after controlling for age, sex, race, smoking behaviour and concomitant drug therapy was 0.89 (95% confidence interval, 0.45-1.8). It was noted that this estimate of no excess risk was restricted to a hypertensive population over 40 years of age, exposed to hydralazine for various periods (none longer than five years)². Another

study involving women with breast cancer also showed no increased risk with use of hydralazine (relative risk, 0.9; 0.5-1.7)³.

B. Evidence for carcinogenicity to animals (*limited*)

Hydralazine hydrochloride was tested in one experiment in mice by oral administration. A significant increase in the incidence of lung tumours was reported¹.

C. Other relevant data

No data were available on the genetic and related effects of hydralazine in humans.

In a single, limited study, hydralazine did not induce DNA damage in animals treated *in vivo*. It induced sister chromatid exchanges in human lymphocytes *in vitro*, whereas assays for chromosomal aberrations in rodent cells *in vitro* were inconclusive. Hydralazine induced unscheduled DNA synthesis in rat and rabbit hepatocytes *in vitro* and induced mutation and DNA damage in bacteria⁴.

References

¹IARC Monographs, 24, 85-100, 1980

²Rogers, A.S. (1984) Hydralazine: an estimate of cancer risk in a hypertensive program (Abstract). *Diss. Abstr. int.*, 44, 2123

³Kaufman, D.W., Kelly, J.P., Rosenberg, L., Stolley, P.D., Schottenfeld, D. & Shapiro, S. (1987) Hydralazine and breast cancer. *J. natl Cancer Inst.*, 78, 243-246

⁴IARC Monographs, Suppl. 6, 338-340, 1987