

after this period, however, had very little effect on the cerebellar weight and little effect on the behavior of the animals when measured postnatally. For example, maze learning and avoidance behavior were not affected [Holson et al., 1997b]. The authors concluded that exposure to retinoic acid at doses near lethal for survival during a period of maximum sensitivity to retinoids does not cause severe learning deficits. This activity decreased for exposure at times after the sensitive period [Holson et al., 1997a].

In acute oral toxicity studies in 2-week old rats, no clinical signs were observed at doses less than 308 mg/kg [Hoffmann-La Roche data on file].

5.7.4 Summary

In summary, although the role of retinoic acid in the developing CNS is well characterized, extrapolation to effects on the mature brain seem unwarranted.

5.8 Overall Conclusions on Psychiatric Conditions

As the preceding sections demonstrate, analysis of all available data (pharmacoepidemiological, retrospective studies, and prospective studies), failed to confirm the initial signal of an association between Accutane and psychiatric morbidity.

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