Methylphenidate and Its Salts

Methylphenidate and its salts, such as methylphenidate hydrochloride (Ritalin), are commonly prescribed psycho-stimulants used in the treatment of attention deficit/hyperactivity disorder in children and adults. Methylphenidate is also used to treat narcolepsy.

Methylphenidate and its salts passed the animal data screen, underwent a preliminary toxicological evaluation, and are being brought to the Carcinogen Identification Committee for consultation. This is a compilation of the relevant studies identified during the preliminary toxicological evaluation.

Epidemiological data

- Cohort studies
    - Elevated standardized morbidity ratio for lymphocytic leukemia in child methylphenidate users
    - No increase in cancer risk in subjects receiving methylphenidate

Animal carcinogenicity data

- Two-year dietary studies
  - Male and female B6C3F1 mice: NTP (1995)
    - Liver tumors (by pairwise comparison and trend) in males and females
    - No treatment-related tumor findings

- Transgenic mouse studies
  - 24-week dietary studies in male and female transgenic p53(+/-) mice: Freeman et al. (1998)
    - No treatment-related tumor findings
  - 24-week dietary studies in male and female Tg.AC transgenic mice: Freeman et al. (1998)
    - No treatment-related tumor findings
Other relevant data

- Genotoxicity
  - SCE, CA, and MN in lymphocytes of exposed children (positive and negative): El-Zein et al. (2005); Witt et al. (2008); Ponsa et al. (2009); Walitza et al. (2010)
  - DNA damage in rat cells in vivo (positive and negative): Andreazza et al. (2007); Witt et al. (2010)
  - Sister chromatid exchanges (SCE) and chromosome aberrations (CA) in Chinese hamster ovary cells (positive): NTP (1995, p. 5, 56); NTP (2005, pp. II-34 – II-35)
  - Induction of unscheduled DNA synthesis in rat hepatocytes in vitro (negative): Mirsalis et al. (1983)
  - Mutations in Big Blue mice in vivo (negative): Manjanatha et al. (2009)
  - HIS49 Pig-A mutations in red blood cells of rats exposed in vivo (negative): Dobrovolsky et al. (2010)
  - Micronuclei (MN) in mouse bone marrow and peripheral blood erythrocytes in vivo (negative): NTP (2005, p. II-35); Manjanatha et al. (2009)
  - MN in rat blood cells in vivo (negative): Andreazza et al. (2007); Dobrovolsky et al. (2010); Witt et al. (2010)
  - HPRT mutation, MN, and CA in male rhesus monkeys in vivo (negative): Morris et al. (2009)

- Mechanistic considerations
  - CA as a biomarker of cancer risk: Bonassi et al. (2008)

References


---

1 Excerpts or the complete publication have been provided to members of the Carcinogen Identification Committee, in the order in which they are discussed in this document.


