Iron Dextran Complex

CAS No. 9004-66-4

Reasonably anticipated to be a human carcinogen

First listed in the *Second Annual Report on Carcinogens* (1981)

Also known as Infed, a registered trademark of Watson Pharma, Inc.

Carcinogenicity

Iron dextran complex is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in experimental animals.

Cancer Studies in Experimental Animals

Exposure to iron dextran by injection caused tumors at the injection site in several species of experimental animals. Cancer at the injection site (sarcoma) was observed following administration of iron dextran complex by subcutaneous injection in mice of both sexes and in male rats and by intramuscular injection in rats and rabbits of both sexes (IARC 1973, 1982).

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to iron dextran complex. There have been case reports of cancer occurring at the sites where iron dextran was thought to have been injected (IARC 1973, Greenberg 1976). Since iron dextran complex was listed in the *Second Annual Report on Carcinogens,* many epidemiological studies have evaluated the carcinogenicity of exposure to iron; however, these studies did not specifically examine exposure to iron dextran complex (Huang 2003).

Properties

Iron dextran complex is a chemical complex of iron hydroxide with dextrans, (polysaccharides that are produced by bacterial action on sugar) (IARC 1973). Iron dextran is a slightly viscous, dark reddish-brown liquid at room temperature (HSDB 2009). When used as a hematinic to treat iron-deficiency anemia in humans or animals, it is prepared as a dark-brown colloidal suspension in saline solution (IARC 1973). The veterinary product generally is more concentrated than the one intended for use in humans. Iron dextran complex is extremely soluble in water and insoluble in most organic solvents. It is unstable at higher temperatures and undergoes autoxidation between 65°C and 70°C (Akron 2009). Its shelf life is about five years.

Use

Iron dextran complex was first used in the United States in 1957. It is used for parenteral treatment of iron-deficiency anemia, but generally only in special cases, such as when oral treatment has failed. In 1960, approval to use iron dextran complex to treat iron-deficiency anemia in humans in the United States was withdrawn after studies in mice and rats demonstrated that repeated subcutaneous and intramuscular injections caused cancer at the injection site. However, in 1962, the use of iron dextran complex to treat iron-deficiency anemia in humans was reintroduced, as the risk of cancer in humans was thought to be small. Iron dextran complex is also used in veterinary medicine to treat baby pigs (IARC 1973, HSDB 2009).

Production

Iron dextran complex is produced by two manufacturers each in Europe and India and one manufacturer each in the United States and Canada (SRI 2009) and is available from six suppliers, including two in the United States (ChemSources 2009). Three products containing iron dextran complex are approved for use by the U.S. Food and Drug Administration (FDA 2009). No data on U.S. imports or exports of iron dextran were found.

Exposure

The primary routes of human exposure to iron dextran complex are intravenous or deep-intramuscular injection (IARC 1973, HSDB 2009). Iron dextran is available as an injectable product in 50-mg vials (FDA 2009). The therapeutic dose for humans is based on body weight and hemoglobin when administered for iron-deficiency anemia and on blood loss and hematocrit when given for blood loss (RxList 2010). The usual daily dose is 1 to 5 mL (50 to 250 mg of iron) (IARC 1973). Use is advised only for patients who do not respond to oral administration of iron. Before 2000, nearly all parenterally administered iron supplements were iron dextran products; however, the use of iron dextran has since diminished, while use of other iron products and the use of injectable iron supplements as a class have increased (Bailie *et al.* 2005). From 2001 to 2003, about 30 million doses of iron supplements were administered by injection, 9.3 million of which were brand-name iron dextran products (Chertow *et al.* 2006). The physician's package insert for iron dextran includes a warning of the potential for injection-site sarcoma (RxList 2010).

Occupational exposure to iron dextran complex may occur during the production, formulation, packaging, or administration of the pharmaceutical products. The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 1,157 workers, including 573 women, potentially were exposed to iron dextran complex (NIOSH 1990). Exposure during production may be site-limited, because only one manufacturer of iron dextran was identified in the United States in 2009 (SRI 2009).

Regulations

Food and Drug Administration (FDA)

Iron dextran complex is a prescription drug subject to labeling and other requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH)

A comprehensive set of guidelines has been established to prevent occupational exposures to hazardous drugs in health-care settings.

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