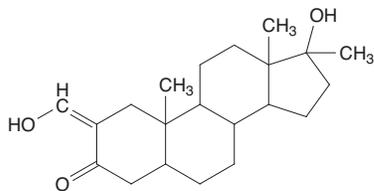


Oxymetholone

CAS No. 434-07-1

Reasonably anticipated to be a human carcinogen

First listed in the *First Annual Report on Carcinogens* (1980)



Carcinogenicity

Oxymetholone is *reasonably anticipated to be a human carcinogen* based on limited evidence of carcinogenicity in humans.

Cancer Studies in Humans

There is limited evidence for the carcinogenicity of oxymetholone in humans. In numerous case reports, liver tumors have been reported in patients with aplastic anemia, Fanconi anemia, paroxysmal nocturnal hemoglobinuria, or other disorders who were treated, usually for long periods, with oxymetholone alone or in combination with other androgenic drugs; however, a causal relationship cannot be firmly established (IARC 1977).

Since oxymetholone was listed in the *First Annual Report on Carcinogens*, additional case reports, primarily of liver cancer, have been identified. Some of the reports were of patients with Fanconi anemia who developed leukemia, liver cancer, or esophageal cancer following oxymetholone treatment (IARC 1987, Linares *et al.* 1991); Fanconi anemia patients are at increased risk for acute myeloid leukemia and squamous-cell carcinoma of the head, neck, and anogenital regions (Auerbach 2009). Case reports of liver cancer and one report of bile-duct cancer (ampullary carcinoma) also have been reported in patients undergoing oxymetholone treatment for other conditions (Kosaka *et al.* 1996, Nakao *et al.* 2000, Fujino *et al.* 2001, Socas *et al.* 2005).

Cancer Studies in Experimental Animals

No adequate studies in experimental animals were available at the time oxymetholone was listed in the *First Annual Report on Carcinogens*. Since then, a cancer study in rats has been identified. Administration of oxymetholone by stomach tube increased the combined incidence of benign and malignant liver tumors (hepatocellular adenoma and carcinoma) in female rats. Benign lung tumors and benign and malignant skin tumors in female rats also were considered to be related to oxymetholone exposure (NTP 1999)

Properties

Oxymetholone is a synthetic anabolic steroid that is structurally related to the male hormone testosterone (IARC 1977, NTP 1999). It exists at room temperature as white-to-creamy crystals (Akron 2009, NTP 1999). It is practically insoluble in water, but it is soluble in ethanol, dioxane, and ether and very soluble in chloroform (HSDB 2009). It is sensitive to light (Akron 2009). Physical and chemical properties of oxymetholone are listed in the following table.

Property	Information
Molecular weight	332.5 ^a
Melting point	178°C to 180°C ^a
Log K_{ow}	3.61 ^b
Water solubility	5.21 mg/L at 25°C ^a
Vapor pressure	5.1×10^{-11} mm Hg at 25°C ^a
Dissociation constant (pK_a)	4.5 ^c

Sources: ^aHSDB 2009, ^bChemIDplus 2009, ^cAkron 2009.

Use

Oxymetholone and other synthetic androgens are used to treat a variety of conditions, including hypogonadism and delayed puberty. Androgens are also used to correct hereditary angioneurotic edema, manage breast cancer, promote a positive nitrogen balance following injury or surgery, and stimulate production of red blood cells. Considerable amounts of androgens are consumed by athletes in attempts to improve athletic performance. Oxymetholone is used to promote weight gain and counteract weakness and emaciation resulting from debilitating diseases, such as advanced HIV infection, and after serious infections, burns, trauma, or surgery. It is marketed as a human prescription drug for the treatment of anemia caused by deficient red-blood-cell production. It has also been used in veterinary medicine as an anabolic steroid for small animals. In 1972, the U.S. Food and Drug Administration permitted the use of oxymetholone to treat pituitary dwarfism and as an adjunctive therapy in osteoporosis pending further investigation (NTP 1999). The FDA withdrew its approval for use of oxymetholone in the treatment of pituitary dwarfism in 1980 and in topically applied drug products for over-the-counter use in 1993 (FDA 2010). In 1983, the FDA allowed the continued use of oxymetholone for treatment of "certain anemias" (NTP 1999).

Production

There is no evidence that oxymetholone has ever been produced commercially in the United States (IARC 1977). In 2009, no producers of oxymetholone were identified worldwide (SRI 2009), but it was available from 14 suppliers, including 8 U.S. suppliers (ChemSources 2009). In 1977, U.S. sales of oxymetholone for use in human medicine were estimated to be less than 44 lb annually (IARC 1977). No data on U.S. exports or imports were found specifically for oxymetholone. U.S. imports of all "anabolic agents and androgens" were 35,000 lb in 2000, but no data on U.S. imports or exports in this category since 2001 were found (USITC 2009).

Exposure

The primary routes of potential human exposure to oxymetholone are ingestion and dermal contact (FDA 2009, HSDB 2009). Oxymetholone is administered to children and adults at dosages of 1 to 5 mg/kg of body weight per day for treatment of anemia caused by deficient red-blood-cell production (Pavlatos *et al.* 2001). A regimen of 100 mg twice a day is recommended as an effective dose for HIV wasting (Hengge *et al.* 2003).

Since the 1950s, increasing numbers of athletes have used anabolic steroid drugs in efforts to increase strength (NTP 1999). In the 1980s, it was estimated that 80% to 100% of national and international male bodybuilders, weightlifters, and participants in the shot put, discus, hammer, and javelin throws used anabolic steroids; football players and competitors in other sports used anabolic steroids to a lesser extent. It has been estimated that more than 1 million individuals abuse steroids in the United States (Hall and Hall 2005). Most abusers start using steroids by age 16. It has been reported that between 4% and 12% of male high-school students and 0.5% to 2.5% of female high-

school students abuse steroids (Riem and Hursey 1995). Dosages used by athletes are often much higher than the normal endogenous testosterone production of 4 to 10 mg per day. Documented daily dosages range from 10 or 15 to 300 mg, with anecdotal reports of up to 2 g. Internet sites that sell anabolic steroids state that male athletes typically take oxymetholone at daily dosages of 50 to 150 mg (Zupplements 2010). Generally, a variety of injectable and oral steroids are taken at dosages that increase, peak, and then taper off prior to competitions and potential drug tests (NTP 1999).

Health professionals such as pharmacists, physicians, and nurses may potentially be exposed while dispensing or administering drug products containing oxymetholone. The risk of occupational exposure during production is low, since the oxymetholone is not produced in the United States (HSDB 2009). The National Occupational Exposure Survey (conducted from 1981 to 1983) estimated that 742 workers, including 359 women, potentially were exposed to oxymetholone (NIOSH 1990).

Regulations

Consumer Product Safety Commission (CPSC)

Any orally administered prescription drug for human use requires child-resistant packaging.

Food and Drug Administration (FDA, an HHS agency)

Oxymetholone is a prescription drug subject to labeling and other requirements.

Guidelines

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

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

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

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

References

- Akron. 2009. *The Chemical Database*. The Department of Chemistry at the University of Akron. <http://ull.chemistry.uakron.edu/erd> and search on CAS number. Last accessed: 8/14/09.
- Auerbach AD. 2009. Fanconi anemia and its diagnosis. *Mutation Res* 668: 4-10.
- ChemDplus. 2009. *ChemDplus Advanced*. National Library of Medicine. <http://chem.sis.nlm.nih.gov/chemidplus/chemidheavy.jsp> and select Registry Number and search on CAS number. Last accessed: 8/14/09.
- ChemSources. 2009. *Chem Sources - Chemical Search*. Chemical Sources International. <http://www.chemsources.com/chemonline.html> and search on oxymetholone. Last accessed: 8/14/09.
- FDA. 2009. *The Electronic Orange Book*. U.S. Food and Drug Administration. <http://www.fda.gov/cder/ob/default.htm> and select Search by Active Ingredient and search on oxymetholone. Last accessed: 8/14/09.
- FDA. 2010. *Title 21: Food and Drugs. Chapter 1: Food and Drug Administration, Department of Health and Human Services. Subchapter D: Drugs for Human Use. Part 310: New Drugs*. U.S. Government Printing Office, Code of Federal Regulations. Last updated: 6/4/10. <http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=e79fcdad8c71d2ff485e564c28aa47&rgn=div8&view=text&node=21:5.0.1.1.2.5.1.12&idno=21>.
- Fujino Y, Ku Y, Suzuki Y, Ajiki T, Hasegawa Y, Kuroda Y. 2001. Ampullary carcinoma developing after androgenic steroid therapy for aplastic anemia: Report of a case. *Surgery* 129(4): 501-503.
- Hall RCW, Hall RCW. 2005. Abuse of supraphysiologic doses of anabolic steroids. *South Med J* 98(5): 550-555.
- Hengge UR, Stocks K, Faulkner S, Wiehler H, Lorenz C, Jentzen W, Hengge D, Ringham G. 2003. Oxymetholone for the treatment of HIV-wasting: A double-blind, randomized, placebo-controlled phase III trial in eugonadal men and women. *HIV Clin Trials* 4(3): 150-163.
- HSDB. 2009. *Hazardous Substances Data Bank*. National Library of Medicine. <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB> and search on CAS number. Last accessed: 8/14/09.
- IARC. 1977. Oxymetholone. In *Some Miscellaneous Pharmaceutical Substances*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, vol. 13. Lyon, France: International Agency for Research on Cancer. pp. 131-140.
- IARC. 1987. Androgenic (anabolic) steroids. In *Overall Evaluations of Carcinogenicity*. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, suppl. 7. Lyon, France: International Agency for Research on Cancer. pp. 96-99.
- Kosaka A, Takahashi H, Yajima Y, Tanaka M, Okamura K, Mizumoto R, Katsuta K. 1996. Hepatocellular carcinoma associated with anabolic steroid therapy: Report of a case and review of the Japanese literature. *J Gastroenterol* 31(3): 450-454.
- Linares M, Pastor E, Gomez A, Grau E. 1991. Hepatocellular carcinoma and squamous cell carcinoma in a patient with Fanconi's anemia. *Ann Hematol* 63(1): 54-55.
- Nakao A, Sakagami K, Nakata Y, Komazawa K, Amimoto T, Nakashima K, Isozaki H, Takakura N, Tanaka N. 2000. Multiple hepatic adenomas caused by long-term administration of androgenic steroids for aplastic anemia in association with familial adenomatous polyposis. *J Gastroenterol* 35(7): 557-562.
- NIOSH. 1990. *National Occupational Exposure Survey (1981-83)*. National Institute for Occupational Safety and Health. Last updated: 7/1/90. <http://www.cdc.gov/noes/noes1/x6172sic.html>.
- NTP. 1999. *Toxicology and Carcinogenesis Studies of Oxymetholone (CAS No. 434-07-1) in F344/N Rats and Toxicology Studies of Oxymetholone in B6C3F₁ Mice (Gavage Studies)*. Technical Report Series no. 485. Research Triangle Park, NC: National Toxicology Program. 240 pp.
- Pavlatos AM, Fultz O, Monberg MJ, Vootkur A, Pharmd. 2001. Review of oxymetholone: A 17 α -alkylated anabolic-androgenic steroid. *Clin Ther* 23(6): 789-801; discussion 771.
- Riem KE, Hursey KG. 1995. Using anabolic-androgenic steroids to enhance physique and performance: Effects on moods and behavior. *Clin Psychol Rev* 15(3): 235-256.
- Socas L, Zumbado M, Perez-Luzardo O, Ramos A, Perez C, Hernandez JR, Boada LD. 2005. Hepatocellular adenomas associated with anabolic androgenic steroid abuse in bodybuilders: A report of two cases and a review of the literature. *Br J Sports Med* 39(5): e27.
- SRI. 2009. *Directory of Chemical Producers*. Menlo Park, CA: SRI Consulting. Database edition. Last accessed: 8/14/09.
- USITC. 2009. *USITC Interactive Tariff and Trade DataWeb*. United States International Trade Commission. http://dataweb.usitc.gov/scripts/user_set.asp and search on HTS no. 2937999510.
- Zupplements. 2010. *Anabolic Steroid Profiles*. Zupplements.com. http://www.zupplements.com/steroids/all_steroid_profiles.htm. Last accessed: 6/21/10.