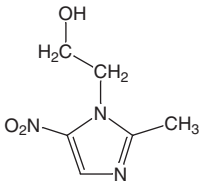
# Metronidazole
# CAS No. 443-48-1

Reasonably anticipated to be a human carcinogen
First Listed in the *Fourth Annual Report on Carcinogens* (1985)




## Carcinogenicity

Metronidazole is *reasonably anticipated to be a human carcinogen* based on sufficient evidence of carcinogenicity in experimental animals (IARC 1977, 1982, 1987). When administered orally, metronidazole induced an increased incidence of lung tumors in mice of both sexes and lymphomas in female mice. Oral administration of the compound also caused mammary fibroadenomas and adenocarcinomas, and pituitary, testicular, and liver tumors in rats (IARC 1977, 1982, 1987).

There is inadequate evidence for the carcinogenicity of metronidazole in humans (IARC 1982, 1987). Two epidemiological studies of women treated with metronidazole showed an excess of uterine cervical cancers, a neoplasm that has risk factors in common with vaginal trichomoniasis (for which metronidazole is administered). In one study, a greater excess of cervical cancer was observed in women with trichomoniasis who were not exposed to metronidazole compared to those who were exposed. One of the two epidemiological studies showed an excess of lung cancer; however, further analysis indicated that this excess could be due to smoking (IARC 1977).

## Properties

Metronidazole occurs as white to pale-yellow crystals or a crystalline powder. It has a molecular weight of 171.2 and melts at 158°C to 160°C. It is soluble in water, ethanol, ether, chloroform, and dilute acids, and sparingly soluble in dimethylformamide. Its octanol/water partition coefficient is -0.02 at 25°C (HSDB 2001).

## Use

Metronidazole is used primarily as a drug for the treatment of infections due to *Entamoeba histolytica, Trichomonas vaginalis,* and *Giardia lamblia*. Metronidazole has also been used to treat Vincent's infection and acne rosacea. It has been prescribed for invasive intestinal amoebiasis or amoebic hepatic abscess. Metronidazole can also be used as a trichomonacidal agent in veterinary medicine (IARC 1977). Metronidazole may be administered orally (capsules or tablets), topically (gels or creams), or by injection (Medlineplus 2001).

## Production

Commercial production of metronidazole in the United States was first reported in 1963 (IARC 1977). In 1974, only one firm reported producing metronidazole in the United States In 1977, total U.S. sales of metronidazole were estimated to be less than 28,600 lb annually (IARC 1977). Currently, twelve U.S. companies supply metronidazole, but current production data and information on imports or exports were not found (Chem Sources 2001).

## Exposure

The primary routes of potential human exposure to metronidazole are ingestion or topical application of the drug for treatment of certain infectious diseases. A recommended oral dose regime is 750 mg three times per day for 5 to 10 days. As a systemic trichomonacidal agent, metronidazole is typically administered in a dose regimen of 250 mg orally three times per day for 7 days. When used to treat giardiasis, metronidazole is administered in a daily dose of 500 mg for 5 days and repeated if necessary. Metronidazole has also been applied in pessaries in a dose of 500 mg daily for 10 to 20 days, indicating that small populations of women potentially experience vaginal or uterine exposure to the compound. Potential occupational exposure may occur through inhalation and dermal contact for workers involved in the manufacture, formulation, packaging, or administration of metronidazole (IARC 1977).

## Regulations

**CPSC**

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

**FDA**

Metronidazole is a prescription drug subject to labeling and other requirements

### REFERENCES

ChemSources. 2001. Chemical Sources International, Inc. http://www.chemsources.com.

HSDB. 2001. Hazardous Substances Data Base. National Library of Medicine. http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB.

IARC. 1977. 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. 255 pp.

IARC. 1982. Chemicals, Industrial Processes and Industries Associated with Cancer in Humans. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 4. Lyon, France: International Agency for Research on Cancer. 292 pp.

IARC. 1987. Overall Evaluations of Carcinogenicity. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans, Supplement 7. Lyon, France: International Agency for Research on Cancer. 440 pp.

MEDLINEplus. 2001. Drug Information. http://www.nlm.nih.gov/medlineplus/.