

TRAZODONE HYDROCHLORIDE

CASRN: 25332-39-2

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Human Health Effects:

Human Toxicity Excerpts:

/HUMAN EXPOSURE STUDIES/ One patient who intentionally ingested 7.5 g of trazodone experienced only drowsiness and weakness; the patient was aroused at the time of hospitalization and emesis was induced. Another patient had an uneventful recovery after ingesting 9.2 g of trazodone. There have been several reports of accidental ingestion in children; however, the exact amounts ingested are unknown. Each of these children exhibited only lethargy and drowsiness, and recoveries were uneventful. Fatalities have occurred in adults who intentionally ingested trazodone and other drugs (e.g., alcohol, chloral hydrate, amobarbital, chlordiazepoxide, meprobamate) concurrently. /Salt not specified/

[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2273]

PEER REVIEWED

/CASE REPORTS/ Seizures & hyponatremia followed an overdose of trazodone. The patient survived. Severe cardiac toxicity (sinus bradycardia, prolonged QTc interval, torsade de pointes, cardiac arrest), coma, & renal failure led to death after a significant overdose (4.5 g) of trazodone. Respiratory depression is most common in the presence of other CNS depressants, but respiratory arrest has been reported following 2.2 & 3.0 g of trazodone. /Salt not specified/

[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 630] **PEER REVIEWED**

/CASE REPORTS/ Three trazodone related fatalities had blood trazodone concns ranging from 0.96-4.56 ug/mL. /Salt not specified/

[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 631] **PEER REVIEWED**

/CASE REPORTS/ ... A 46-yr-old HIV-positive man with a past medical history of iv drug abuse & hepatitis C, who was well controlled with HIV medications, was admitted for cocaine withdrawal. The patient was started on a standard protocol at the detoxification center with methadone 50 mg/day, clonidine 0.1 mg twice daily for 4 days, & trazodone 200 mg/day for 4 days. Laboratory results showed acute hepatitis & cholestasis 5 days following admission. Trazodone & clonidine were discontinued at that time. His methadone & HIV regimens remained unchanged. Liver function test results were greatly improved 10 days after trazodone & clonidine discontinuation. ... This is the first case report of trazodone-induced liver damage after only a few days of therapy. Previous reports describe hepatitis developing after wks to months of trazodone therapy. All comorbidities thought to affect the described laboratory abnormalities were ruled out as a cause by a hepatologist. The observation of the sudden rise & fall of liver enzymes is characteristic of a drug reaction in the absence of trauma & severe shock. ... Due to the temporal relationship of the introduction & withdrawal of trazodone in the medication regimen & the elevations in liver enzymes, we conclude that this patient

experienced acute hepatitis induced by trazodone 200 mg/day therapy for 4 days. The findings of this case warrant caution & closer monitoring in a patient with multiple risk factors for liver damage. /Salt not specified/

[Rettman KS, McClintock C; Ann Pharmacother 35(12): 1559-1561 (2001)] **PEER REVIEWED** [PubMed Abstract](#)

/CASE REPORTS/ A fatal case of suicide with trazodone alone in a 40-yr-old patient is reported. Life-threatening arrhythmias, such as torsades de pointes & complete AV block, are recorded. Blood collected at admission contained a trazodone toxic concn of 25.4 micrograms/ml. The patient developed multiple organ failure & died <24 hrs after his admission to the emergency department. /Salt not specified/

[de Meester A, et al; Acta Clin Belg 56(4): 258-261 (2001)] **PEER REVIEWED** [PubMed Abstract](#)

/CASE REPORTS/ ... We report a case of priapism which occurred following trazodone overdose in an individual actively using cocaine. ... /Salt not specified/

[Myrick H, et al; Ann Clin Psychiatry 10(2): 81-83 (1998)] **PEER REVIEWED** [PubMed Abstract](#)

/CASE REPORTS/ A 79-year-old woman in the course of a syncope evaluation is shown to have a trazodone-related cardiac arrhythmia confirmed by drug rechallenge. This nontricyclic antidepressant should be considered as potentially arrhythmogenic despite its generally favorable cardiovascular profile. /Salt not specified/

[Vitullo RN et al; Chest 98 (1): 247-248 (1990)] **PEER REVIEWED** [PubMed Abstract](#)

/BIOMONITORING/ The pharmacology & forensic toxicology of trazodone & ...toxicology & cause & manner of death in a series of 37 deaths in which trazodone was detected /are reviewed/. Although the normal upper therapeutic blood concn for trazodone is about 2 mg/l, fatalities are rarely attributed solely to it at blood concns below 9 mg/l. Considering the pharmacology of the drug, potential interactions between other drugs with serotonin reuptake properties need to be considered, as does the increased susceptibility to the toxic effects in patients with pre-existing heart disease. In the cases reviewed, none were attributed solely to trazodone, although trazodone was frequently present together with other serotonergic drugs, such as the selective serotonin reuptake inhibitors like fluoxetine & sertraline. Ten cases had blood trazodone concns above 2 mg/l. Of these cases, trazodone played a primary role in the death of 3 subjects, with blood concns all >9 mg/l. We confirm the conclusions of others that trazodone is a relatively safe drug except in massive overdose, although its toxicity may be influenced by the presence of other drugs & underlying pathophysiology. /Salt not specified/

[Goeringer KE, et al; J Forensic Sci 45 (4): 850-856 (2000)] **PEER REVIEWED** [PubMed Abstract](#)

Drug Warnings:

There is a decr in m-chlorophenylpiperazine clearance with age due to decline of renal function. mCPP clearance is dependent on renal & left ventricular cardiac function. /from table/ /Salt not specified/

[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 620] **PEER REVIEWED**

Elderly patients are more likely than younger adults to experience the sedative or hypotensive effect of trazodone; therefore, initial doses as low as half the recommended adult dose should be used in elderly

patients, with adjustment made as needed and tolerated. /Salt not specified/

[MICROMEDEX Thomson Health Care. USPDI - Drug Information for the Health Care Professional. 22nd ed. Volume 1. MICROMEDEX Thomson Health Care, Greenwood Village, CO. 2002. Content Reviewed and Approved by the U.S. Pharmacopeial Convention, Inc., p. 2831]
PEER REVIEWED

Adverse nervous system effects occur frequently during the first few weeks of therapy with trazodone. The most frequent adverse effect associated with trazodone therapy is drowsiness, which occurs in 20-50% of patients receiving the drug. Other less frequent adverse nervous system effects of trazodone include dizziness and lightheadedness, nervousness, fatigue, malaise, weakness, heaviness or fullness of the head, headache, and insomnia. Confusion, incoordination, anger or hostility, agitation, decreased concentrating ability, impaired memory, impaired speech, disorientation, hallucinations or delusions, and excitement have also occurred. Hypomania, nightmares or vivid dreams, tonic-clonic seizures, tremors, paresthesias, and akathisia occur rarely. /Salt not specified/

[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Although bothersome anticholinergic effects commonly occur with tricyclic antidepressants, these effects appear to occur less frequently with trazodone. Dry mouth has been reported in about 15-30% of patients during trazodone therapy; it has been suggested that this effect may result from an alpha-adrenergic blocking effect rather than an anticholinergic effect of trazodone. In several placebo-controlled studies, the incidence of dry mouth was similar in trazodone- & placebo-treated patients. Other anticholinergic effects such as blurred vision, constipation, and urinary retention have been reported less frequently. /Salt not specified/

[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Trazodone therapy has been associated with priapism, with surgical intervention required in approximately one-third of reported cases; in some cases, permanent impairment of erectile function or impotence has resulted. Male patients receiving trazodone who experience prolonged or inappropriate penile erections should immediately discontinue the drug and consult their physician. ... Decreased or increased libido, retrograde ejaculation, impotence, inhibited female orgasm (anorgasmia), increased urinary frequency, delayed urine flow, and hematuria have also been associated with trazodone therapy. /Salt not specified/

[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Adverse GI effects of trazodone include nausea and vomiting, dysgeusia, and abdominal and gastric disorders. Flatulence and diarrhea have also been reported. /Salt not specified/

[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Trazodone is thought to be less cardiotoxic than currently available tricyclic antidepressant agents. Hypotension (including orthostatic hypotension) is the most frequent adverse cardiovascular effect of trazodone, occurring in about 5% of patients receiving the drug. In most patients, hypotension is mild and not dose related. Syncope, shortness of breath, chest pain, tachycardia, palpitations, and hypertension have also occurred. Bradycardia has occurred in a few patients during long-term therapy. /Salt not specified/

[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda,

MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Various ECG changes have occurred in patients receiving trazodone. In patients with preexisting cardiac disease, trazodone may be arrhythmogenic. PVCs, ventricular couplets, and short episodes (3 or 4 beats) of ventricular tachycardia have occurred in these patients. Arrhythmias have also been reported in patients without preexisting cardiac disease. Cardiac arrest has also been reported. Myocardial infarction has been reported, but this effect has not been attributed directly to trazodone. /Salt not specified/
[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Occasional decreases in leukocyte and neutrophil counts have occurred in some patients receiving trazodone. These changes were not considered clinically important and did not require discontinuance of the drug. Anemia has also been associated with trazodone therapy in a few patients. /Salt not specified/
[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Musculoskeletal aches and pains have occurred in about 5% of patients receiving trazodone. A few patients have developed muscle twitches. Pruritus, rash, urticaria, acne, photosensitivity, edema, nasal or sinus congestion, eye irritation, sweating or clamminess, early or absent menses, and tinnitus have been reported in some patients receiving trazodone. Allergic reactions and hypersalivation have rarely occurred. Minimal increases in serum concentrations of alkaline phosphatase, AST (SGOT), and ALT (SGPT) have occurred in some patients receiving trazodone. /Salt not specified/
[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Patients should be warned that trazodone may impair their ability to perform activities requiring mental alertness or physical coordination (e.g., operating machinery, driving a motor vehicle). Patients also should be warned that trazodone may enhance their response to alcohol, barbiturates, or other CNS depressants. Since the risk of dizziness or lightheadedness may be increased during fasting conditions, patients should be advised to take trazodone shortly after a meal or light snack. In addition, total drug absorption may be up to 20% greater when the drug is taken with food rather than on an empty stomach. Because priapism has been associated with trazodone therapy, patients should be instructed to discontinue the drug and consult a physician if prolonged or inappropriate penile erection occurs. /Salt not specified/
[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2272]
PEER REVIEWED

Until additional clinical experience on the safety of trazodone in patients with cardiovascular disease is obtained, it is recommended that these patients be closely monitored, particularly for arrhythmias, while receiving the drug. ... It is also recommended that trazodone not be used during the initial recovery phase of myocardial infarction. /Salt not specified/
[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2273]
PEER REVIEWED

Leukocyte and differential counts should be performed in patients who develop fever and sore throat or other

signs of infection while receiving trazodone. The drug should be discontinued in patients whose leukocyte or absolute neutrophil count decreases to less than normal levels. /Salt not specified/

[McEvoy, G.K. (ed.). American Hospital Formulary Service- Drug Information 2002. Bethesda, MD: American Society of Health-System Pharmacists, Inc. 2002 (Plus Supplements)., p. 2273] **PEER REVIEWED**

Side effects of trazodone include: moderately severe sedation; moderate GI effects; minimal cardiac effects; & mild priapism. /from table/ /Salt not specified/

[Hardman, J.G., L.E. Limbird, P.B., A.G. Gilman. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw-Hill, 2001., p. 455] **PEER REVIEWED**

Trazodone... can produce GI upset, which may be relieved by the coadmin of food. Trazodone also is a potent alpha-adrenergic blocker producing a significant amount of orthostasis. Postural hypotension occurs early in therapy & the elderly are more susceptible to this effect. Additionally, injury following a fall (e.g., hip fracture) is a significant risk factor in the elderly. /Salt not specified/

[Young, L.Y., M.A. Koda-Kimble (eds.). Applied Therapeutics. The Clinical Use of Drugs. 6th ed. Vancouver, WA., Applied Therapeutics, Inc. 1995., p. 76-16] **PEER REVIEWED**

... Three bulimic patients treated with trazodone developed visual hallucinations that resolved within 12-72 hr after decreases in dose or discontinuation of trazodone. /Salt not specified/

[Young, L.Y., M.A. Koda-Kimble (eds.). Applied Therapeutics. The Clinical Use of Drugs. 6th ed. Vancouver, WA., Applied Therapeutics, Inc. 1995., p. 80-5] **PEER REVIEWED**

... Major adverse events for trazodone were sedation & dry mouth, & for valproate, diarrhea, nausea & headaches. /Salt not specified/

[Rickels K, et al; Psychopharmacology (Berl) 141(1): 1-5 (1999)] **PEER REVIEWED** [PubMed Abstract](#)

Trazodone, a triazolepyridine derivate, is both chemically & pharmacologically distinct from other serotonin reuptake inhibitors & possesses antidepressant, anxiolytic & hypnotic activity. We observed trazodone-induced delirium in 3 depressed patients who also suffered from preexisting organic cerebral lesions (2 cases) or thyroidal dysfunction (1 case). The appearance of hallucinations, psychomotoric agitation, & cognitive changes after initiation of trazodone therapy & their prompt cessation after drug discontinuation led to the impression that these were drug-induced phenomena. One possible hypothesis for the observed deliria is an oversensitivity to the effect of meta-chlorophenylpiperazine, which is a metabolite of trazodone with specific 5-HT agonistic properties. /Salt not specified/

[Lennkh C, et al; Int Clin Psychopharmacol 13(5): 225-228 (1998)] **PEER REVIEWED** [PubMed Abstract](#)

Ten depressed patients treated with trazodone developed edema and weight gain that was promptly reversed by reduction or discontinuation of trazodone. This suggests a dose-dependent effect. None of the patients had an active medical problem that might predispose to edema formation. Summary data on all 10 cases and three case histories are presented to alert physicians to this side effect. /Salt not specified/

[Barnett J et al; J Clin Psychopharmacol 5 (3): 161-164 (1985)] **PEER REVIEWED** [PubMed Abstract](#)

A hemodialysis male patient exhibited depressive symptoms and trazodone was prescribed orally. Although his depressive symptoms disappeared, he gradually presented with parkinsonism. His parkinsonism improved within a week after stopping trazodone. The clinical course strongly suggested that it was induced by

trazodone. However, there is no report on antidopaminergic side effects of parkinsonism. This case suggests that antidopaminergic effects leading to parkinsonism need to be considered in patients on hemodialysis that are taking trazodone. /Salt not specified/

[Fukunishi I et al; Nephron 90 (2): 222-223 (2002)] **PEER REVIEWED** [PubMed Abstract](#)

... Trazodone has been used widely to treat insomnia in depressed patients. When used in combination with electroconvulsive therapy (ECT), trazodone has been suspected to cause cardiovascular side effects. ... A retrospective study was done of 100 patients who received ECT with concurrent trazodone. One patient was excluded because permission to review the patient's records had not been given. The remaining 99 patients were matched with control ECT patients. ... No statistically significant between-group differences were identified in cardiovascular side effects, although a trend toward more orthostatic hypotension was observed in patients taking trazodone. ... Administering low-dose trazodone for insomnia in conjunction with ECT does not appear to incr cardiovascular complications. The true incidence of adverse cardiac events was not higher than 3.66% at a 95% confidence level. /Salt not specified/

[Krahn LE, et al; J Clin Psychiatry 62(2): 108-110 (2001)] **PEER REVIEWED** [PubMed Abstract](#)

Body Burden:

Three trazodone related fatalities had blood trazodone concns ranging from 0.96-4.56 ug/mL. /Salt not specified/

[Ellenhorn, M.J., S. Schonwald, G. Ordog, J. Wasserberger. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. 2nd ed. Baltimore, MD: Williams and Wilkins, 1997., p. 631] **PEER REVIEWED**

A fatal case of suicide with trazodone alone in a 40-yr-old patient is reported. ... Blood collected at admission contained a trazodone toxic concn of 25.4 ug/ml. ... /Salt not specified/

[de Meester A, et al; Acta Clin Belg 56(4): 258-261 (2001)] **PEER REVIEWED** [PubMed Abstract](#)