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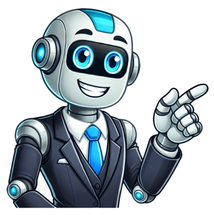

Drug test bzd

Our DNA Legal ongoing series aims to explore the legal implications of drug misuse. We've published articles relating to amphetamines, ketamine, cannabis, cocaine, and tramadol misuse. They're prescribed medications to treat anxiety, panic disorders, and insomnia. Production, supply, and possession are illegal without a prescription. Types of benzodiazepines, commonly known as "benzos", include midazolam, clobazam, and lorazepam. They work by suppressing the central nervous system to slow down the mind and the body's function - abusers use them to induce states of calm and relaxation. As a class C drug controlled by the Misuse of Drugs Act (1971), the possession can result in 2 years in prison and an unlimited fine. Below, we'll answer these questions about benzodiazepine testing: Will benzodiazepines show on a drug test? How long will benzodiazepines stay in your system? What tests will detect benzodiazepines? What factors influence benzodiazepine detection? Why might a court-ordered benzodiazepine test be necessary? What happens if a benzodiazepine test comes back positive? How DNA Legal can help Will Benzodiazepines Show on a Drug Test? 10-panel drug tests will show benzodiazepine use. But not all benzodiazepines will show. There are multiple short, intermediate, and long-acting benzodiazepines. The short and intermediates have the potential not to show on a 10-panel drug. If a court or healthcare professional suspects benzodiazepine misuse, it's essential to perform a test as soon as possible. How Long Will Benzodiazepines Stay in Your System? Benzodiazepines can cause users to feel drowsy, relaxed, calm, confused, or disorientated. They differ from the other drugs we've covered in our ongoing series because there are short to long-term effects depending on the controlled release of the drug. How long it will stay in the different body systems also differs. Here's a table for the type of tests and the average detection times: Body System Short-Acting Intermediate-Acting Long-Acting Urine Up to 24 hours 1-5 days 5-8 days Blood 12-24 hours 12-24 hours 12-24 hours Saliva 2.5 days 2.5 days 2.5 days Fingernails 3-6 months 3-6 months 3-6 months Hair Up to 12 months Up to 12 months Up to 12 months Note: Data varies on detection times. Detection times will also vary depending on the type of benzodiazepine. What Tests Will Detect Benzodiazepines? A court has the option of using the five different tests in the table above. What test they select will depend on the legal scenario. Blood Test: Within 12-24 Hours A blood test is an effective method for legal or healthcare professionals, but the detection window is short. The test should typically be performed as close to an offence as possible if benzodiazepine abuse is detected. Professionals can provide a more accurate picture by using a blood test alongside a urine test. Urine Test: Within 8 Days A urine test is one of the most common and effective court-ordered drug tests for benzodiazepines if attempting to detect drug misuse within a shorter time frame. They're one of the most accurate tests that can determine the type of benzodiazepine use, but detection varies depending on the type of benzodiazepine and the amount taken. Rapid Saliva Test: Within 2.5 Days The rapid saliva test is more effective for benzodiazepines than other drugs - the detection length is longer. The rapid saliva test will also reveal any drug use within roughly 30 minutes, making it one of the best tests to select if court-directed testing requires rapid results. Fingernails Test: Within 3 to 6 Months For a court-ordered drug test in scenarios like a child custody dispute, a fingernail test is effective because it can detect long-term drug abuse. A fingernail test works because traces of benzodiazepine become trapped within the keratin fibres and stay until the nail grows out. Hair Test: Within 12 months A hair drug test works similarly to a fingernail drug test - traces of benzodiazepines remain trapped in the keratin fibres of the hair for up to 6 months. Using a sample of hair can be a more effective and accurate form of detection for long-term benzodiazepine abuse, but it depends on the growth of the hair. Each 1 cm segment of hair represents approximately one month depending on hair growth rates (as it can vary). Legal and healthcare professionals must wait 2 - 3 weeks (depending on hair growth rate) before testing, so it's not the test of choice for rapid detection. What Factors Influence Benzodiazepine Detection? Numerous factors influence benzodiazepine detection: Frequency of consumption Age Weight Hydration levels Metabolism The type of benzodiazepine Typically, detection varies from person to person. Whether it was a street-manufactured or medically manufactured benzodiazepine also makes a difference. Street 'brands' have unregulated doses and content. Why Might a Court-Ordered Benzodiazepine Test Be Necessary? A court will order a benzodiazepine drug test for clarity when supporting a case. If it's a child custody case, benzodiazepine misuse by a parent or caregiver could result in harm to the well-being or health of the child. A test is also useful for legal officials at the time of an offence if they suspect benzodiazepine misuse - for example, a road traffic accident. What Happens if a Benzodiazepine Test Comes Back Positive? The consequences will depend on the legal case. For a child custody case, a positive result could lead to limited or terminated visitation and custody rights. If there's no prescription, the legal consequences are listed above relating to potential prison time and fines. That said, some court cases will present drug misusers with the chance to attend regular court-ordered drug rehabilitation. Anyone willing to do so could face lighter charges in the court case. How DNA Legal can help At DNA Legal, we have nearly 20 years of experience assisting individuals with the drug testing process. Our trained professionals can help whether you need the test to support a legal or personal case. We understand the stress being required to take a drug test can cause - we're here to support and guide you through it all. Monitoring for opioid-related problems, largely through urine drug testing, has become a central component of risk mitigation in long-term opioid therapy. Many people with addictive disorders go to hospital emergency rooms because they're in crisis. Most hospitals provide an evaluation and assess the patient's primary need and then connect him or her to the right treatment that best addresses their unique needs. Many general hospitals don't admit patients solely for withdrawal or substance abuse treatment unless there is some other factor such as a significant other medical problem presents. Opiate dependence is a brain-related medical disorder that can be effectively treated with significant benefits for the patient and society. Substance use disorders can be best treated on an outpatient therapy basis, or in an inpatient program dedicated to the treatment of people with addiction. Many of these programs use medications to help patients transition from physical dependence on opioids. What Does MTD Mean On A Drug Test? Some of the terminologies used in drug testing reports can be confusing because the drugs are represented by color codes and abbreviations. MTD in drug testing stands for Methadone a category of drugs called opioids. German doctors created it during World War II. When it came to the United States, doctors used it to treat people with extreme pain. Methadone changes the way the brain and nervous system respond to pain so that patients feel relief. Its effects are slower than those of other strong painkillers like morphine. It also blocks the high from drugs like codeine, heroin, hydrocodone, morphine, and oxycodone. It can give a similar feeling and keep people from having withdrawal symptoms and cravings. Methadone maintenance treatment has been used to treat opioid dependence since the 1950s. The opioid-dependent patient takes a daily dose of methadone as a liquid or pill. This reduces their withdrawal symptoms and cravings for opioids. Clinical opinions about how long methadone stay in your system vary anywhere from 2 days to up to 13 days. While methadone is typically processed out of your system within two weeks, traces of the drug can show up for much longer, depending on the type of drug test used. Employers, addiction treatment programs, athletic organizations, and law enforcement officials may all request methadone drug tests. While standard drug tests often test for opioid use, such as heroin, codeine, and morphine, they do not pick up on methadone use. Because of this, specific and more costly tests must be used if the drug test is screening for methadone use. Urine, saliva, hair, and blood tests have all been developed to test for the presence of methadone in the system. Methadone is addictive, like other opioids. However, being on methadone is not the same as being dependent on illegal opioids such as heroin: It is safer for the patient to take methadone under medical supervision than it is to take heroin of unknown purity. Methadone is taken orally. Heroin is often injected, which can lead to HIV transmission if needles and syringes are shared. People who are heroin-dependent often spend most of their time trying to obtain and use heroin. This can involve criminal activity such as stealing. Patients in methadone do not need to do this. Instead, they can undertake productive activities such as education, employment, and parenting. Methadone has been included on the World Health Organization's List of Essential Medicines. This highlights its importance as a treatment for heroin dependence. What is a Methadone Clinic? A methadone clinic is a clinic for the dispensing of methadone (Dolophine), a schedule II opioid analgesic to a person who is addicted to opioid-based drugs, such as heroin or prescription painkillers. What Does a Methadone Clinic Do? The main focus of methadone clinics is the elimination or reduction of opioid usage by placing the patient on methadone which is a long-acting opioid that blocks the effects of opiate pain medications, including morphine, codeine, oxycodone, and other semi-synthetic opioids. According to the Journal of Addiction Science & Clinical Practice, the purpose of methadone treatment works to restore a normal chemical balance within the brain while supporting damaged neurotransmitter-producing cells. Once the brain's chemical environment stabilizes, a person starts to feel normal again in terms of his or her emotional and psychological well-being. All methadone clinics in the United States are strictly regulated by state and federal laws and administer methadone as a pill, in liquid or wafer forms. A common term for this type of treatment at a methadone clinic which must be prescribed by a doctor is known as is "replacement therapy". Although considered successful as a treatment method it is not a cure for addiction issues and the use of this maintenance treatment is often viewed as controversial in many quarters. The American Journal of Psychology says the DSM-5 manual, which doctors use to diagnose mental health disorders, describes methadone as a safe substance for treating substance use disorders. How Much Does It Cost to Go To A Methadone Clinic? Methadone clinics could either be public or privately owned. In either case, they both come under the same strict regulations that guide their operations (inpatient and outpatient levels of care). While not restricted to adults, this treatment method is generally not considered for people under the age of 18. In 2013, due to the strict changes in receiving prescription pain medication as well as decreases in prescription abuse, the requirements to be accepted into methadone clinics have changed in areas such as New York State. The average cost of a non-hospital-based residential Methadone treatment program is $76.13 per day per person, while persons visiting a Methadone clinic on an out-patient basis should expect to pay an average cost of $17.78 per day per person. According to a survey conducted by the Substance Abuse and Mental Health Services Administration, nearly 245,000 people were admitted into opiate treatment programs in 2010. More than half of those admitted required maintenance and detoxification services. About 22 percent were individuals seeking only maintenance treatment. Methadone was the primary medication given to those in treatment; the survey reported nearly 270,000 people receiving methadone in March of the following year. READ: How Long Does Suboxone Strips Stay In Your System Who is Eligible for Methadone Replacement Therapy? The first step in getting methadone maintenance is to get assessed in a clinic by a methadone doctor. Anyone seeking help for opiate addiction can receive an assessment for methadone maintenance although there may be limitations to what the clinic will be able to do for you especially public methadone clinics with limited budget. In General, assessment for methadone maintenance involves providing accurate and up-to-date information about yourself to the staff members of the clinic. If you are not completely honest about other drugs you are using, you could be placing yourself at risk for an accidental overdose. Required information includes: Demographic information (age, sex, date of birth). Medical history: including any diseases transmitted through sexual intercourse or through shared needles. Psychiatric history: including mental health disorders such as anxiety, depression, and psychosis. Risk assessment: including information about past or present thoughts of suicide or suicide attempts. Past and current drug use: this may include a detailed report of the drugs that you have used in the last month up to one year. History of withdrawal symptoms (experienced currently or in the past). In addition to the information above, it is particularly important to be honest about your use of other central nervous system depressants, such as: benzodiazepines, barbiturates, and sleep medications (e.g., Ambien) alcohol, and other opiates. How does Methadone Clinics Operate? Methadone clinics will not provide you with methadone maintenance without your complete and voluntary informed consent. The consent process will include you signing that you understand the facility services, procedures, rules, and expectations. By signing, you agree to conduct yourself in the manner outlined by the facility. However, in cases where you are considered a risk to yourself or others and are referred to a 72-hour hold, your right to willingly provide treatment consent is lost and treatment can commence without your consent. Methadone clinics work in such a way that on the day of your initial assessment, you will probably receive your first treatment as long as you are eligible and there are no persons on the waiting list. Your initial dosage will not exceed 40 mg methadone but will be slowly increased over the next few weeks with a final dosage goal of anywhere from 80 to 120 mg under close supervision. Once clinic staff and ''Methadone Doctors" are satisfied with your progress you will transition to outpatient treatment who visits the clinic every day to receive your supervised daily dosage. Based on your level of commitment and sincerity in the methadone, the methadone facility may entrust you with dosages of up to 4 weeks at a time. The duration of methadone treatment ranges from a few months to several years, or even lifelong. Some clinics also offer short- or long-term detoxification services to their patients using methadone in combination with cognitive behavioral therapy and other medications such as buprenorphine used to reduce cravings, naltrexone, a non-addictive substance, that blocks the effects of opioids and the injectable form of naltrexone, known as Vivitrol, that is administered monthly rather than daily like most other opioid treatment drugs. Factors That Affect Duration of Methadone Treatment Several factors affect methadone treatment duration most of which are related to your history of drug use and current state. These factors include: Length of opiate abuse, as in months, years, or decades The presence or absence of mental health problems, such as depression, anxiety, or bipolar disorders Whether or not a person has a strong support system in place Stable vs. unstable home environment Side Effects to Expect During Methadone Treatment Although carefully monitored dosages of methadone are legally and medically acceptable, methadone is still an opioid agonist drug like heroin or opium. It is important to recognize that, while methadone is a milder drug, it is still a narcotic with a high chance of addiction and dangerous side effects. When a person takes methadone in any form, they run the risk of experiencing a host of dangerous effects, which can cause both physical and psychological harm. The side effects of methadone include: Labored or shallow breathing Nausea/vomiting, Diarrhea and Abdominal cramps How to find the Right Methadone Clinic Near You In many parts of the United States, methadone clinics are few and far between, which presents problems for addicts seeking methadone treatment who live far from a clinic. By simply typing 'methadone clinic near me' on a search engine, a number of online resources for finding local methadone clinics will pop up but finding the right one could be much harder. One way you can find the right methadone clinic is by searching state or city-wise and principally by reading customer reviews on methadone clinics. Another reliable method you can get the required help in locating the right methadone clinic for you is by referral. Public methadone clinics are generally cheaper to attend. However, they are usually crowded with a long waiting list due to limited funding. The private methadone clinics, on the other hand, are more expensive to attend but usually have either a short or no waiting list with a more personalized form of care. Other methadone clinics cater for specific demographic groups such as gender or religion to maximize the comfort of their clients. Canadian Methadone Treatment Centers Ontario Addiction Treatment Centre No reviews · Medical Clinic Bracebridge, ON, Canada · +1 705-645-1677 Opens 8:30 AM Fri OATC Vanier Clinic Addiction Treatment Center Vanier, ON, Canada · +1 613-749-9666 Opens 8:30 AM Fri WEBSITE Methadone Clinic & Pharmacy Addiction Treatment Center Toronto, ON, Canada · +1 416-241-5281 Open · Closes 6:30 PM Ontario Addiction Treatment Centre Medical Clinic Bracebridge, ON, Canada · +1 705-645-1677 Opens 8:30 AM Fri To find a Methadone Clinic Near me click on either of the site below; Clinic Location Finder Site 1 Clinic Location Finder Site 2 A drug test looks for the presence of one or more illegal or prescription drugs in your urine, blood, saliva, hair, or sweat. Urine testing is the most common type of drug screening. Other names of this analysis include; drug screen, drug test, drugs of abuse testing, substance abuse testing, toxicology screen, tox screen, sports doping tests. One of the major challenges of urine drug testing is adulteration, a practice involving manipulation of a urine specimen with chemical adulterants to produce a false negative test result. This problem is compounded by the number of easily obtained chemicals that can effectively adulterate a urine specimen. What happens during a drug test? A drug test generally requires that you give a urine sample in a lab. You will be given instructions to provide a "clean catch" sample. The clean catch method includes the following steps: Clean your genital area with a cleansing pad given to you by your provider. Men should wipe the tip of their penis. Women should open their labia and clean from front to back. Start to urinate into the toilet. Move the collection container under your urine stream. Collect at least an ounce or two of urine into the container, which should have markings to indicate the amounts. Finish urinating into the toilet. Return the sample container to the lab technician or health care provider. In certain instances, a medical technician or other staff member may need to be present while you provide your sample. Can they legally watch you pee for a drug test? Usually not. Some courts have found it to be an unfair invasion of privacy to watch employees urinate. However, most courts have held that it is reasonable to enforce other safeguards that protect against tampering with urine specimens. What is it used for? Drug screening is used to find out whether or not a person has taken a certain drug or drugs. It may be used for: Employment. Employers may test you before hiring and/or after hiring to check for on-the-job drug use. Sports organizations. Professional and collegiate athletes usually need to take a test for performance-enhancing drugs or other substances. Legal or forensic purposes. Testing may be part of a criminal or motor vehicle accident investigation. Drug screening may also be ordered as part of a court case. Monitoring opioid use. If you've been prescribed an opioid for chronic pain, your health care provider may order a drug test to make sure you are taking the right amount of your medicine. Why do I need a drug test? You may have to take a drug test as a condition of your employment, in order to participate in organized sports, or as part of a police investigation or court case. Your health care provider may order drug screening if you have symptoms of drug abuse. These symptoms include: Changes in blood pressure or heart rhythm For a blood test for drugs, you will go to a lab to provide your sample. During the test, a health care professional will take a blood sample from a vein in your arm, using a small needle. After the needle is inserted, a small amount of blood will be collected into a test tube or vial. You may feel a little sting when the needle goes in or out. This usually takes less than five minutes. Will I need to do anything to prepare for the test? Be sure to tell the testing provider or your health care provider if you are taking any prescription drugs, over-the-counter medicines, or supplements because they may give you a positive result for certain illegal drugs. Also, you should avoid foods with poppy seeds, which can cause a positive result for opioids. What do the results mean? If your results are negative, it means no drugs were found in your body, or the level of drugs was below an established level, which differs depending on the drug. If your results are positive, it means one or more drugs were found in your body above an established level. However, false positives can happen. So if your first test shows that you have drugs in your system, you will have further testing to figure out whether or not you are actually taking a certain drug or drugs. Can you put Visine in your urine to pass a drug test? Attempts to dilute, adulterate, and substitute urine may be detected by visual inspection and laboratory validity testing. Validity testing of urine specimens includes temperature, specific gravity, pH, urine creatinine, and presence of adulterants. Urine temperature within 4 minutes of voiding should range from 90°F to 100°F in a healthy individual, whereas temperatures outside of this range may suggest a substituted specimen has been provided. Many specimen cups have a temperature gauge on the side of the cup. A specimen outside of the physiological range should be recollected. Urine samples are sometimes contaminated deliberately by ingestion or addition of a foreign substance to prevent detection of illicit drugs. Common methods of tampering include dilution with water, addition of extraneous substances, or substitution of samples. Studies reveal that at low concentrations of Visine, false-negative cannabinoid results were attributable to the benzalkonium chloride ingredient of Visine. The added Visine was not detectable by routine urine analysis and had no effect on the activity of the glucose-6-phosphate dehydrogenase-drug conjugate used in the assays. It is important to note that putting Visine eye drops in your urine cannot help you pass a drug test because even when contaminated with Visine, analysis by gas chromatography/mass spectrometry will reveal any drug present in the Visine-adulterated urine specimens. Are there any risks to the test? There are no known physical risks to having a drug test, but a positive result may affect other aspects of your life, including your job, your eligibility to play sports, and the outcome of a court case. Before you take a drug test, you should be told what you are being tested for, why you are being tested, and how the results will be used. If you have questions or concerns about your test, talk to your health care provider or contact the individual or organization that ordered the test. SEE: What Does Mop Mean On A Drug Test? Class of depressant drugs "Benzo" redirects here. For other uses, see Benzo (disambiguation). BenzodiazepinesDrug classStructural formula of benzodiazepines.Class identifiersUseAnxiety disorders, seizures, muscle spasms, panic disorderATC codeN05BAMode of actionGABAA receptorClinical dataWebMDMedicineNet RxListExternal linksMeSHD001569Legal statusIn Wikidata Benzodiazepines (BZD, BDZ, BZs), colloquially known as "benzos", are a class of central nervous system (CNS) depressant drugs whose core chemical structure is the fusion of a benzene ring and a diazepine ring. They are prescribed to treat conditions such as anxiety disorders, insomnia, and seizures. The first benzodiazepine, chlordiazepoxide (Librium), was discovered accidentally by Leo Sternbach in 1955, and was made available in 1960 by Hoffmann–La Roche, which followed with the development of diazepam (Valium) three years later, in 1963.[1] By 1977, benzodiazepines were the most prescribed medications globally; the introduction of selective serotonin reuptake inhibitors (SSRIs), among other factors, decreased rates of prescription, but they remain frequently used worldwide.[2][3] Benzodiazepines are depressants that enhance the effect of the neurotransmitter gamma-aminobutyric acid (GABA) at the GABAA receptor, resulting in sedative, hypnotic (sleep-inducing), anxiolytic (anti-anxiety), anticonvulsant, and muscle relaxant properties. High doses of many shorter-acting benzodiazepines may also cause anterograde amnesia and dissociation.[4] These properties make benzodiazepines useful in treating anxiety, panic disorder, insomnia, agitation, seizures, muscle spasms, alcohol withdrawal and as a premedication for medical or dental procedures.[5] Benzodiazepines are categorized as short, intermediate, or long-acting. Short- and intermediate-acting benzodiazepines are preferred for the treatment of insomnia; longer-acting benzodiazepines are recommended for the treatment of anxiety.[6] Benzodiazepines are generally viewed as safe and effective for short-term use of two to four weeks,[7] although cognitive impairment and paradoxical effects such as aggression or behavioral disinhibition can occur.[8] According to the Government of Victoria's (Australia) Department of Health, long-term use can cause "impaired thinking or memory loss, anxiety and depression, irritability, paranoia, aggression, etc."[9] A minority of people have paradoxical reactions after taking benzodiazepines such as worsened agitation or panic.[8] Benzodiazepines are often prescribed for as-needed use, which is under-studied, but probably safe and effective to the extent that it involves intermittent short-term use.[10] Benzodiazepines are associated with an increased risk of suicide due to aggression, impulsivity, and negative withdrawal effects.[11] Long-term use is controversial because of concerns about decreasing effectiveness, physical dependence, benzodiazepine withdrawal syndrome, and an increased risk of dementia and cancer.[12][13][14][15] The elderly are at an increased risk of both short- and long-term adverse effects,[16][17] and as a result, all benzodiazepines are listed in the Beers List of inappropriate medications for older adults.[18] There is controversy concerning the safety of benzodiazepines in pregnancy. While they are not major teratogens, uncertainty remains as to whether they cause cleft palate in a small number of babies and whether neurobehavioural effects occur as a result of prenatal exposure;[19] they are known to cause withdrawal symptoms in the newborn. In an overdose, benzodiazepines can cause dangerous deep unconsciousness, but are less toxic than their predecessors, the barbiturates, and death rarely results when a benzodiazepine is the only drug taken. Combined with other central nervous system (CNS) depressants such as alcohol and opioids, the potential for toxicity and fatal overdose increases significantly.[20][21] Benzodiazepines are commonly used recreationally and also often taken in combination with other addictive substances, and are controlled in most countries.[22][23][24] See also: List of benzodiazepines Midazolam 1 & 5 mg/mL injections (Canada) Benzodiazepines possess psycholeptic, sedative, hypnotic, anxiolytic, anticonvulsant, muscle relaxant, and amnesic actions,[4][5] which are useful in a variety of indications such as alcohol dependence, seizures, anxiety disorders, panic, agitation, and insomnia. Most are administered orally; however, they can also be given intravenously, intramuscularly, or rectally.[25]:189 In general, benzodiazepines are well tolerated and are safe and effective drugs in the short term for a wide range of conditions.[26][27] Tolerance can develop to their effects and there is also a risk of dependence, and upon discontinuation a withdrawal syndrome may occur. These factors, combined with other possible secondary effects after prolonged use such as psychomotor, cognitive, or memory impairments, limit their long-term applicability.[28][29] The effects of long-term use or misuse include the tendency to cause or worsen cognitive deficits, depression, and anxiety.[16][17] The College of Physicians and Surgeons of British Columbia recommends discontinuing the usage of benzodiazepines in those on opioids and those who have used them long term.[30] Benzodiazepines can have serious adverse health outcomes, and these findings support clinical and regulatory efforts to reduce usage, especially in combination with non-benzodiazepine receptor agonists.[31] Further information: Panic disorder Because of their effectiveness, tolerability, and rapid onset of anxiolytic action, benzodiazepines are frequently used for the treatment of anxiety associated with panic disorder.[32] However, there is disagreement among expert bodies regarding the long-term use of benzodiazepines for panic disorder. The views range from those holding benzodiazepines are not effective long-term[33] and should be reserved for treatment-resistant cases[34] to those holding they are as effective in the long term as selective serotonin reuptake inhibitors (SSRIs).[35] American Psychiatric Association (APA) guidelines, published in January 2009,[35] note that, in general, benzodiazepines are well tolerated, and their use for the initial treatment for panic disorder is strongly supported by numerous controlled trials. APA states that there is insufficient evidence to recommend any of the established panic disorder treatments over another. The choice of treatment between benzodiazepines, SSRIs, serotonin–norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants, and psychotherapy should be based on the patient's history, preference, and other individual characteristics. Selective serotonin reuptake inhibitors are likely to be the best choice of pharmacotherapy for many patients with panic disorder, but benzodiazepines are also often used, and some studies suggest that these medications are still used with greater frequency than the SSRIs. One advantage of benzodiazepines is that they alleviate the anxiety symptoms much more quickly than antidepressants, and therefore may be preferred in patients for whom rapid symptom control is critical. However, this advantage is offset by the possibility of developing benzodiazepine dependence. APA does not recommend benzodiazepines for persons with depressive symptoms or a recent history of substance use disorder. APA guidelines state that, in general, pharmacotherapy of panic disorder should be continued for at least a year, and that clinical experience supports continuing benzodiazepine treatment to prevent recurrence. Although major concerns about benzodiazepine tolerance and withdrawal have been raised, there is no evidence for significant dose escalation in patients using benzodiazepines long-term. For many such patients, stable doses of benzodiazepines retain their efficacy over several years.[35] Guidelines issued by the UK-based National Institute for Health and Clinical Excellence (NICE), carried out a systematic review using different methodology and came to a different conclusion. They questioned the accuracy of studies that were not placebo-controlled. And, based on the findings of placebo-controlled studies, they do not recommend use of benzodiazepines beyond two to four weeks, as tolerance and physical dependence develop rapidly, with withdrawal symptoms including rebound anxiety occurring after six weeks or more of use.[33][36] Nevertheless, benzodiazepines are still prescribed for long-term treatment of anxiety disorders, although specific antidepressants and psychological therapies are recommended as the first-line treatment options with the anticonvulsant drug pregabalin indicated as a second- or third-line treatment and suitable for long-term use.[37] NICE stated that long-term use of benzodiazepines for panic disorder with or without agoraphobia is an unlicensed indication, does not have long-term efficacy, and is, therefore, not recommended by clinical guidelines. Psychological therapies such as cognitive behavioural therapy are recommended as a first-line therapy for panic disorder; benzodiazepine use has been found to interfere with therapeutic gains from these therapies.[33] Benzodiazepines are usually administered orally; however, very occasionally lorazepam or diazepam may be given intravenously for the treatment of panic attacks.[25] Further information: Generalized anxiety disorder Benzodiazepines have robust efficacy in the short-term management of generalized anxiety disorder (GAD) when standardized measures of anxiety are used as the outcome variable,[38] but did not demonstrate a favorable dropout rate compared to placebo in one meta-analysis.[39] A newer meta-analysis showed that benzodiazepines are significantly more effective than serotonergic agents, regardless of treatment length.[40] More research is needed, but unfortunately, newer randomized controlled trials are scarce for the off patent benzodiazepines. According to National Institute for Health and Clinical Excellence (NICE), benzodiazepines can be used in the immediate management of GAD, if necessary. However, they should not usually be given for longer than 2–4 weeks. The only medications NICE recommends for the longer term management of GAD are antidepressants.[41] Likewise, Canadian Psychiatric Association (CPA) recommends benzodiazepines alprazolam, bromazepam, lorazepam, and diazepam only as a second-line choice, if the treatment with two different antidepressants was unsuccessful.[42] Although they are second-line agents, benzodiazepines can be used for a limited time to relieve severe anxiety and agitation. CPA guidelines state that after 4–6 weeks the effect of benzodiazepines may decrease to the level of placebo,[42] and that benzodiazepines are less effective than antidepressants in alleviating ruminative worry, the core symptom of GAD, but that in some cases, a prolonged treatment with benzodiazepines as the add-on to an antidepressant may be justified. Evidence from reviews of benzodiazepine tolerance mechanisms[43] and clonazepam use in psychiatric disorders[44] is strongly discordant with the claim that benzodiazepines lose anxiolytic efficacy over a period of weeks, as these reviews present RCT evidence of continued anxiolytic efficacy at up to 22 weeks[45] and observational (open-label) evidence of continued efficacy at up to 3 years.[46] A 2015 review found a larger effect with medications than talk therapy.[47] Medications with benefit include serotonin-noradrenaline reuptake inhibitors, benzodiazepines, and selective serotonin reuptake inhibitors.[47] Further information: Insomnia Temazepam (Normison) 10 mg tablets Benzodiazepines can be useful for short-term treatment of insomnia. Their use beyond 2 to 4 weeks is not recommended due to the risk of dependence. The Committee on Safety of Medicines report recommended that where long-term use of benzodiazepines for insomnia is indicated then treatment should be intermittent wherever possible.[48] It is preferred that benzodiazepines be taken intermittently and at the lowest effective dose. They improve sleep-related problems by shortening the time spent in bed before falling asleep, prolonging the sleep time, and, in general, reducing wakefulness.[49][50] However, they worsen sleep quality by increasing light sleep and decreasing deep sleep. Other drawbacks of hypnotics, including benzodiazepines, are possible tolerance to their effects, rebound insomnia, and reduced slow-wave sleep and a withdrawal period typified by rebound insomnia and a prolonged period of anxiety and agitation.[51][52] The list of benzodiazepines approved for the treatment of insomnia is fairly similar among most countries, but which benzodiazepines are officially designated as first-line hypnotics prescribed for the treatment of insomnia varies between countries.[50] Longer-acting benzodiazepines such as nitrazepam and diazepam have residual effects that may persist into the next day and are, in general, not recommended.[49] Since the release of nonbenzodiazepines, also known as z-drugs, in 1992 in response to safety concerns, individuals with insomnia and other sleep disorders have increasingly been prescribed nonbenzodiazepines (2.3% in 1993 to 13.7% of Americans in 2010), less often prescribed benzodiazepines (23.5% in 1993 to 10.8% in 2010).[53][54] It is not clear as to whether the new non benzodiazepine hypnotics (Z-drugs) are better than the short-acting benzodiazepines. The efficacy of these two groups of medications is similar.[49][52] According to the US Agency for Healthcare Research and Quality, indirect comparison indicates that side-effects from benzodiazepines may be about twice as frequent as from nonbenzodiazepines.[52] Some experts suggest using nonbenzodiazepines preferentially as a first-line long-term treatment of insomnia.[50] However, the UK National Institute for Health and Clinical Excellence did not find any convincing evidence in favor of Z-drugs. NICE review pointed out that short-acting Z-drugs were inappropriately compared in clinical trials with long-acting benzodiazepines. There have been no trials comparing short-acting Z-drugs with appropriate doses of short-acting benzodiazepines. Based on this, NICE recommended choosing the hypnotic based on cost and the patient's preference.[49] Older adults should not use benzodiazepines to treat insomnia unless other treatments have failed.[55] When benzodiazepines are used, patients, their caretakers, and their physician should discuss the increased risk of harms, including evidence that shows twice the incidence of traffic collisions among driving patients, and falls and hip fracture for older patients.[55][56][57] Further information: Seizure Prolonged convulsive epileptic seizures are a medical emergency that can usually be dealt with effectively by administering fast-acting benzodiazepines, which are potent anticonvulsants. In a hospital environment, intravenous clonazepam, lorazepam, and diazepam are first-line choices. In the community, intravenous administration is not practical and so rectal diazepam or buccal midazolam are used, with a preference for midazolam as its administration is easier and more socially acceptable.[58][59] When benzodiazepines were first introduced, they were enthusiastically adopted for treating all forms of epilepsy. However, drowsiness and tolerance become problems with continued use and none are now considered first-line choices for long-term epilepsy therapy.[60] Clobazam is widely used by specialist epilepsy clinics worldwide and clonazepam is popular in the Netherlands, Belgium and France.[60] Clobazam was approved for use in the United States in 2011. In the UK, both clobazam and clonazepam are second-line choices for treating many forms of epilepsy.[61] Clobazam also has a useful role for very short-term seizure prophylaxis and in catamenial epilepsy.[60] Discontinuation after long-term use in epilepsy requires additional caution because of the risks of rebound seizures. Therefore, the dose is slowly tapered over a period of up to six months or longer.[59] Further information: Alcohol detoxification Chlordiazepoxide is the most commonly used benzodiazepine for alcohol detoxification,[62] but diazepam may be used as an alternative. Both are used in the detoxification of individuals who are motivated to stop drinking, and are prescribed for a short period of time to reduce the risks of developing tolerance and dependence to the benzodiazepine medication itself.[25]:275 The benzodiazepines with a longer half-life make detoxification more tolerable, and dangerous (and potentially lethal) alcohol withdrawal effects are less likely to occur. On the other hand, short-acting benzodiazepines may lead to breakthrough seizures, and are, therefore, not recommended for detoxification in an outpatient setting. Oxazepam and lorazepam are often used in patients at risk of drug accumulation, in particular, the elderly and those with cirrhosis, because they are metabolized differently from other benzodiazepines, through conjugation.[63][64] Benzodiazepines are the preferred choice in the management of alcohol withdrawal syndrome, in particular, for the prevention and treatment of the dangerous complication of seizures and in subduing severe delirium.[65] Lorazepam is the only benzodiazepine with predictable intramuscular absorption and it is the most effective in preventing and controlling acute seizures.[66] Benzodiazepines are often prescribed for a wide range of conditions: They can sedate patients receiving mechanical ventilation or those in extreme distress. Caution is exercised in this situation due to the risk of respiratory depression, and it is recommended that benzodiazepine overdose treatment facilities should be available.[67] They have also been found to increase the likelihood of later PTSD after people have been removed from ventilators.[68] Benzodiazepines are indicated in the management of breathlessness (shortness of breath) in advanced diseases, in particular where other treatments have failed to adequately control symptoms.[69] Benzodiazepines are effective as medication given a couple of hours before surgery to relieve anxiety. They also produce amnesia, which can be useful, as patients may not remember unpleasantness from the procedure.[70] They are also used in patients with dental phobia as well as some ophthalmic procedures like refractive surgery; although such use is controversial and only recommended for those who are very anxious.[71] Midazolam is the most commonly prescribed for this use because of its strong sedative actions and fast recovery time, as well as its water solubility, which reduces pain upon injection. Diazepam and lorazepam are sometimes used. Lorazepam has particularly marked amnesic properties that may make it more effective when amnesia is the desired effect.[25]:693 Benzodiazepines are well known for their strong muscle-relaxing properties and can be useful in the treatment of muscle spasms,[25]:577–578 although tolerance often develops to their muscle relaxant effects.[16] Baclofen[72] or tizanidine are sometimes used as an alternative to benzodiazepines. Tizanidine has been found to have superior tolerability compared to diazepam and baclofen.[73] Benzodiazepines are also used to treat the acute panic caused by hallucinogen intoxication.[74] Benzodiazepines are also used to calm the acutely agitated individual and can, if required, be given via an intramuscular injection.[75] They can sometimes be effective in the short-term treatment of psychiatric emergencies such as acute psychosis as in schizophrenia or mania, bringing about rapid tranquillization and sedation until the effects of lithium or neuroleptics (antipsychotics) take effect. Lorazepam is most commonly used but clonazepam is sometimes prescribed for acute psychosis or mania;[76] their long-term use is not recommended due to risks of dependence.[25]:204 Further research investigating the use of benzodiazepines alone and in combination with antipsychotic medications for treating acute psychosis is warranted.[77] Clonazepam, a benzodiazepine is used to treat many forms of parasomnia.[78] Rapid eye movement behavior disorder responds well to low doses of clonazepam.[79][80] Restless legs syndrome can be treated using clonazepam as a third line treatment option as the use of clonazepam is still investigational.[81][82] Benzodiazepines are sometimes used for obsessive–compulsive disorder (OCD), although they are generally believed ineffective for this indication. Effectiveness was, however, found in one small study.[83] Benzodiazepines can be considered as a treatment option in treatment resistant cases.[84] Antipsychotics are generally a first-line treatment for delirium; however, when delirium is caused by alcohol or sedative hypnotic withdrawal, benzodiazepines are a first-line treatment.[85] There is some evidence that low doses of benzodiazepines reduce adverse effects of electroconvulsive therapy.[86] Benzodiazepines require special precaution if used in the elderly, during pregnancy, in children, alcohol or drug-dependent individuals and individuals with comorbid psychiatric disorders.[87] Because of their muscle relaxant action, benzodiazepines may cause respiratory depression in susceptible individuals. For that reason, they are contraindicated in people with myasthenia gravis, sleep apnea, bronchitis, and COPD.[88][89] Caution is required when benzodiazepines are used in people with personality disorders or intellectual disability because of frequent paradoxical reactions.[88][89] In major depression, they may precipitate suicidal tendencies[90] and are sometimes used for suicidal overdoses.[89] Individuals with a history of excessive alcohol use or non-medical use of opioids or barbiturates should avoid benzodiazepines, as there is a risk of life-threatening interactions with these drugs.[91] See also: Effects of benzodiazepines on newborns In the United States, the Food and Drug Administration has categorized benzodiazepines into either category D or X meaning potential for harm in the unborn has been demonstrated.[92] Exposure to benzodiazepines during pregnancy has been associated with a slightly increased (from 0.06 to 0.07%) risk of cleft palate in newborns, a controversial conclusion as some studies find no association between benzodiazepines and cleft palate. Their use by expectant mothers shortly before the delivery may result in a floppy infant syndrome. Newborns with this condition tend to have hypotonia, hypothermia, lethargy, and breathing and feeding difficulties.[19][93] Cases of neonatal withdrawal syndrome have been described in infants chronically exposed to benzodiazepines in utero. This syndrome may be hard to recognize, as it starts several days after delivery, for example, as late as 21 days for chlordiazepoxide. The symptoms include tremors, hypertonia, hyperreflexia, hyperactivity, and vomiting and may last for up to three to six months.[19][94] Tapering down the dose during pregnancy may lessen its severity. If used in pregnancy, those benzodiazepines with a better and longer safety record, such as diazepam or chlordiazepoxide, are recommended over potentially more harmful benzodiazepines, such as temazepam[95] or triazolam. Using the lowest effective dose for the shortest period of time minimizes the risks to the unborn child.[96] The benefits of benzodiazepines are least and the risks are greatest in the elderly.[97][98] They are listed as a potentially inappropriate medication for older adults by the American Geriatrics Society.[99] The elderly are at an increased risk of dependence and are more sensitive to the adverse effects such as memory problems, daytime sedation, impaired motor coordination, and increased risk of motor vehicle accidents and falls,[56] and an increased risk of hip fractures.[100] The long-term effects of benzodiazepines and benzodiazepine dependence in the elderly can resemble dementia, depression, or anxiety syndromes, and progressively worsens over time. Adverse effects on cognition can be mistaken for the effects of old age. The benefits of withdrawal include improved cognition, alertness, mobility, reduced risk of incontinence, and a reduced risk of falls and fractures. The success of gradual-tapering benzodiazepines is as great in the elderly as in younger people. Benzodiazepines should be prescribed to the elderly only with caution and only for a short period at low doses.[101][102] Short to intermediate-acting benzodiazepines are preferred in the elderly such as oxazepam and temazepam. The high potency benzodiazepines alprazolam and triazolam and long-acting benzodiazepines are not recommended in the elderly due to increased adverse effects. Nonbenzodiazepines such as zaleplon and zolpidem and low doses of sedating antidepressants are sometimes used as alternatives to benzodiazepines.[102][103] Long-term use of benzodiazepines is associated with increased risk of cognitive impairment and dementia, and reduction in prescribing levels is likely to reduce dementia risk.[14] The association of a history of benzodiazepine use and cognitive decline is unclear, with some studies reporting a lower risk of cognitive decline in former users, some finding no association and some indicating an increased risk of cognitive decline.[104] Benzodiazepines are sometimes prescribed to treat behavioral symptoms of dementia. However, like antidepressants, they have little evidence of effectiveness, although antipsychotics have shown some benefit.[105][106] Cognitive impairing effects of benzodiazepines that occur frequently in the elderly can also worsen dementia.[107] Table from the 2010 ISCD study ranking various drugs (legal and illegal) based on statements by drug-harm experts. Benzodiazepines were found to be the 10th most dangerous drug overall.[108] See also: Long-term effects of benzodiazepines, Paradoxical reaction § Benzodiazepines, and benzodiazepine withdrawal syndrome The most common side-effects of benzodiazepines are related to their sedating and muscle-relaxing action. They include drowsiness, dizziness, and decreased alertness and concentration. Lack of coordination may result in falls and injuries particularly in the elderly.[88][109][110] Another result is impairment of driving skills and increased likelihood of road traffic accidents.[111][112] Decreased libido and erection problems are a common side effect. Depression and disinhibition may emerge. Hypotension and suppressed breathing (hypoventilation) may be encountered with intravenous use.[88][109] Less common side effects include nausea and changes in appetite, blurred vision, confusion, euphoria, depersonalization and nightmares. Cases of liver toxicity have been described but are very rare.[25]:183–189[113] The long-term effects of benzodiazepine use can include cognitive impairment as well as affective and behavioural problems. Feelings of turmoil, difficulty in thinking constructively, loss of sex-drive, agoraphobia and social phobia, increasing anxiety and depression, loss of interest in leisure pursuits and interests, and an inability to experience or express feelings can also occur. Not everyone, however, experiences problems with long-term use.[114][115] Additionally, an altered perception of self, environment and relationships may occur.[116] A study published in 2020 found that long-term use of prescription benzodiazepines is associated with an increase in all-cause mortality among those age 65 or younger, but not those older than 65. The study also found that all-cause mortality was increased further in cases in which benzodiazepines are co-prescribed with opioids, relative to cases in which benzodiazepines are prescribed without opioids, but again only in those age 65 or younger.[117] Compared to other sedative-hypnotics, visits to the hospital involving benzodiazepines had a 66% greater odds of a serious adverse health outcome. This included hospitalization, patient transfer, or death, and visits involving a combination of benzodiazepines and non-benzodiapine receptor agonists had almost four-times increased odds of a serious health outcome.[31] In September 2020, the US Food and Drug Administration (FDA) required the boxed warning be updated for all benzodiazepine medicines to describe the risks of abuse, misuse, addiction, physical dependence, and withdrawal reactions consistently across all the medicines in the class.[118] The short-term use of benzodiazepines adversely affects multiple areas of cognition, the most notable one being that it interferes with the formation and consolidation of memories of new material and may induce complete anterograde amnesia.[88] However, researchers hold contrary opinions regarding the effects of long-term administration. One view is that many of the short-term effects continue into the long-term and may even worsen, and are not resolved after stopping benzodiazepine usage. Another view maintains that cognitive deficits in chronic benzodiazepine users occur only for a short period after the dose, or that the anxiety disorder is the cause of these deficits. While the definitive studies are lacking, the former view received support from a 2004 meta-analysis of 13 small studies.[116][119] This meta-analysis found that long-term use of benzodiazepines was associated with moderate to large adverse effects on all areas of cognition, with visuospatial memory being the most commonly detected impairment. Some of the other impairments reported were decreased IQ, visiomotor coordination, information processing, verbal learning and concentration. The authors of the meta-analysis[119] and a later reviewer[116] noted that the applicability of this meta-analysis is limited because the subjects were taken mostly from withdrawal clinics; the coexisting drug, alcohol use, and psychiatric disorders were not defined; and several of the included studies conducted the cognitive measurements during the withdrawal period. Paradoxical reactions, such as increased seizures in epileptics,[120] aggression, violence, impulsivity, irritability and suicidal behavior sometimes occur.[11] These reactions have been explained as consequences of disinhibition and the subsequent loss of control over socially unacceptable behavior. Paradoxical reactions are rare in the general population, with an incidence rate below 1% and similar to placebo.[8][121] However, they occur with greater frequency in recreational abusers, individuals with borderline personality disorder, children, and patients on high-dosage regimes.[122][123] In these groups, impulse control problems are perhaps the most important risk factor for disinhibition; learning disabilities and neurological disorders are also significant risks. Most reports of disinhibition involve high doses of high-potency benzodiazepines.[121] Paradoxical effects may also appear after chronic use of benzodiazepines.[124] While benzodiazepines may have short-term benefits for anxiety, sleep and agitation in some patients, long-term (i.e., greater than 2–4 weeks) use can result in a worsening of the very symptoms the medications are meant to treat. Potential explanations include exacerbating cognitive problems that are already common in anxiety disorders, causing or worsening depression and suicidality,[125][126] disrupting sleep architecture by inhibiting deep stage sleep,[127] withdrawal symptoms or rebound symptoms in between doses mimicking or exacerbating underlying anxiety or sleep disorders,[125][126] inhibiting the benefits of psychotherapy by inhibiting memory consolidation and reducing fear extinction,[128][129][130] and reducing coping with trauma/stress and increasing vulnerability to future stress.[131] The latter two explanations may be why benzodiazepines are ineffective and/or potentially harmful in PTSD and phobias.[132] Anxiety, insomnia and irritability may be temporarily exacerbated during withdrawal, but psychiatric symptoms after discontinuation are usually less than even while taking benzodiazepines.[125][133] Functioning significantly improves within 1 year of discontinuation.[125][134] Main articles: Benzodiazepine dependence, Benzodiazepine withdrawal syndrome, and post-acute withdrawal syndrome Diazepam 2 mg and 5 mg diazepam tablets, which are commonly used in the treatment of benzodiazepine withdrawal. Tolerance and dependence are risks of chronic benzodiazepine use, and can result in doses within the therapeutic range ceasing to offer meaningful symptomatic relief after prolonged use. Tolerance develops at different rates and to different degrees to the sedative, hypnotic, anticonvulsant, muscle relaxant and anxiolytic effects of benzodiazpines. A review[43] of benzodiazepine tolerance concluded that it "appears that tolerance develops relatively quickly for the sedative and anticonvulsant actions of benzodiazepines, whereas tolerance to anxiolytic and amnesic effects probably does not develop at all", although the included randomized controlled trial evidence[135][45] is limited to 22 weeks. A review of clonazepam in the treatment of psychiatric disorders concluded that there is longitudinal data supporting anxiolytic benefit without tolerance during long-term use,[44] including an open-label study finding continued benefit at 3 years.[46] However, the review concludes that long-term RCT evidence is scant. A study of benzodiazepine sensitivity found that patients treated chronically with alprazolam did not differ from untreated patients in terms of anxiolytic response to diazepam, suggesting a lack of anxiolytic tolerance.[136] However, controversy remains regarding tolerance to anxiolytic effects, with

some publications reporting that there is little evidence of continued efficacy beyond 4–6 months[107] or that dependence phenomena are common.[26][33] However, some of these references were published prior to the in-depth scoping reviews of benzodiazepine tolerance, and lack citations of RCT evidence of tolerance. Studies reporting on voluntary benzodiazepine cessation and withdrawal include patient reports of tolerance and worsening anxiety.[16] The question of tolerance to the amnesic effects of benzodiazepines is, likewise, unclear.[137] Some evidence suggests that partial tolerance does develop, and that, "memory impairment is limited to a narrow window within 90 minutes after each dose".[138] A major disadvantage of benzodiazepines is that tolerance to therapeutic effects develops relatively quickly while many adverse effects persist. Tolerance develops to hypnotic and myorelaxant effects within days to weeks, and to anticonvulsant effects within weeks to months.[125] Therefore, benzodiazepines are unlikely to be effective long-term treatments for sleep. While BZD therapeutic effects may disappear with tolerance, depression and impulsivity with high suicidal risk commonly persist.[125] Several studies have confirmed that long-term benzodiazepines are not significantly different from placebo for sleep,[139][140][141] and question their use for anxiety disorders such as PTSD and OCD.[125][142][143][144] This may explain why patients commonly increase doses over time and many eventually take more than one type of benzodiazepine after the first loses effectiveness.[127][145][146] Additionally, because tolerance to benzodiazepine sedating effects develops more quickly than does tolerance to brainstem depressant effects, those taking more benzodiazepines to achieve desired effects may experience sudden respiratory depression, hypotension or death.[147] Most patients with anxiety disorders and PTSD have symptoms that persist for at least several months,[147] making tolerance to therapeutic effects a distinct problem for them and necessitating the need for more effective long-term treatment (e.g., psychotherapy, serotonergic antidepressants). Chlordiazepoxide 5 mg capsules, which are sometimes used as an alternative to diazepam for benzodiazepine withdrawal. Like diazepam it has a long elimination half-life and long-acting active metabolites. Discontinuation of benzodiazepines or abrupt reduction of the dose, even after a relatively short course of treatment (two to four weeks), may result in two groups of symptoms, rebound and withdrawal. Rebound symptoms are the return of the symptoms for which the patient was treated but worse than before. Withdrawal symptoms are the new symptoms that occur when the benzodiazepine is stopped. They are the main sign of physical dependence.[138] The most frequent symptoms of withdrawal from benzodiazepines are insomnia, gastric problems, tremors, agitation, fearfulness, and muscle spasms.[138] The less frequent effects are irritability, sweating, depersonalization, derealization, hypersensitivity to stimuli, depression, suicidal behavior, psychosis, seizures, and delirium tremens.[148] Severe symptoms usually occur as a result of abrupt or over-rapid withdrawal. Abrupt withdrawal can be dangerous and lead to excitotoxicity, causing damage and even death to nerve cells as a result of excessive levels of the excitatory neurotransmitter glutamate. Increased glutamatergic activity is thought to be part of a compensatory mechanism to chronic GABAergic inhibition from benzodiazepines.[149][150] Therefore, a gradual reduction regimen is recommended.[13] Symptoms may also occur during a gradual dosage reduction, but are typically less severe and may persist as part of a protracted withdrawal syndrome for months after cessation of benzodiazepines.[151] Approximately 10% of patients experience a notable protracted withdrawal syndrome, which can persist for many months or in some cases a year or longer. Protracted symptoms tend to resemble those seen during the first couple of months of withdrawal but usually are of a sub-acute level of severity. Such symptoms do gradually lessen over time, eventually disappearing altogether.[152] Benzodiazepines have a reputation with patients and doctors for causing a severe and traumatic withdrawal; however, this is in large part due to the withdrawal process being poorly managed. Over-rapid withdrawal from benzodiazepines increases the severity of the withdrawal syndrome and increases the failure rate. A slow and gradual withdrawal customised to the individual and, if indicated, psychological support is the most effective way of managing the withdrawal. Opinion as to the time needed to complete withdrawal ranges from four weeks to several years. A goal of less than six months has been suggested,[13] but due to factors such as dosage and type of benzodiazepine, reasons for prescription, lifestyle, personality, environmental stresses, and amount of available support, a year or more may be needed to withdraw.[16][25]:183–184 Withdrawal is best managed by transferring the physically dependent patient to an equivalent dose of diazepam because it has the longest half-life of all of the benzodiazepines, is metabolised into long-acting active metabolites and is available in low-potency tablets, which can be quartered for smaller doses.[153] A further benefit is that it is available in liquid form, which allows for even smaller reductions.[13] Chlordiazepoxide, which also has a long half-life and long-acting active metabolites, can be used as an alternative.[153][154] Nonbenzodiazepines are contraindicated during benzodiazepine withdrawal as they are cross tolerant with benzodiazepines and can induce dependence.[16] Alcohol is also cross tolerant with benzodiazepines and more toxic and thus caution is needed to avoid replacing one dependence with another.[153] During withdrawal, fluoroquinolone-based antibiotics are best avoided if possible; they displace benzodiazepines from their binding site and reduce GABA function and, thus, may aggravate withdrawal symptoms.[155] Antipsychotics are not recommended for benzodiazepine withdrawal (or other CNS depressant withdrawal states) especially clozapine, olanzapine or low potency phenothiazines, e.g., chlorpromazine as they lower the seizure threshold and can worsen withdrawal effects; if used extreme caution is required.[156] Withdrawal from long term benzodiazepines is beneficial for most individuals.[124] Withdrawal of benzodiazepines from long-term users, in general, leads to improved physical and mental health particularly in the elderly; although some long term users report continued benefit from taking benzodiazepines, this may be the result of suppression of withdrawal effects.[16][114] Beyond the well established link between benzodiazepines and psychomotor impairment resulting in motor vehicle accidents and falls leading to fracture; research in the 2000s and 2010s has raised the association between benzodiazepines (and Z-drugs) and other, as of yet unproven, adverse effects including dementia, cancer, infections, pancreatitis and respiratory disease exacerbations.[157] A number of studies have drawn an association between long-term benzodiazepine use and neuro-degenerative disease, particularly Alzheimer's disease.[158] It has been determined that long-term use of benzodiazepines is associated with increased dementia risk, even after controlling for protopathic bias.[14] Some observational studies have detected significant associations between benzodiazepines and respiratory infections such as pneumonia[159][160] where others have not.[161] A large meta-analysis of pre-marketing randomized controlled trials on the pharmacologically related Z-Drugs suggest a small increase in infection risk as well.[162] An immunodeficiency effect from the action of benzodiazepines on GABA-A receptors has been postulated from animal studies.[163][164] A meta-analysis of observational studies has determined an association between benzodiazepine use and cancer, though the risk across different agents and different cancers varied significantly.[15] In terms of experimental basic science evidence, an analysis of carcinogenetic and genotoxicity data for various benzodiazepines has suggested a small possibility of carcinogenesis for a small number of benzodiazepines.[165] The evidence suggesting a link between benzodiazepines (and Z-Drugs) and pancreatic inflammation is very sparse and limited to a few observational studies from Taiwan.[166][167] A criticism of confounding can be applied to these findings as with the other controversial associations above. Further well-designed research from other populations as well as a biologically plausible mechanism is required to confirm this association. Main article: Benzodiazepine overdose Although benzodiazepines are much safer in overdose than their predecessors, the barbiturates, they can still cause problems in overdose.[20] Taken alone, they rarely cause severe complications in overdose;[168] statistics in England showed that benzodiazepines were responsible for 3.8% of all deaths by poisoning from a single drug.[22] However, combining these drugs with alcohol, opiates or tricyclic antidepressants markedly raises the toxicity.[23][169][170] The elderly are more sensitive to the side effects of benzodiazepines, and poisoning may even occur from their long-term use.[171] The various benzodiazepines differ in their toxicity; temazepam appears most toxic in overdose and when used with other drugs.[172][173] The symptoms of a benzodiazepine overdose may include; drowsiness, slurred speech, nystagmus, hypotension, ataxia, coma, respiratory depression, and cardiorespiratory arrest.[170] A reversal agent for benzodiazepines exists, flumazenil (Anexate), itself belonging to the chemical class of benzodiazepines. Its use as an antidote is not routinely recommended because of the high risk of resedation and seizures.[174] In a double-blind, placebo-controlled trial of 326 people, 4 people had serious adverse events and 61% became resedated following the use of flumazenil.[175] Numerous contraindications to its use exist. It is contraindicated in people with a history of long-term use of benzodiazepines, those having ingested a substance that lowers the seizure threshold or may cause an arrhythmia, and in those with abnormal vital signs.[176] One study found that only 10% of the people presenting with a benzodiazepine overdose are suitable candidates for treatment with flumazenil.[177] Left: US yearly overdose deaths involving benzodiazepines.[178] Center: The top line represents the number of benzodiazepine deaths that also involved opioids in the US. The bottom line represents benzodiazepine deaths that did not involve opioids.[178] Right: Chemical structure of the benzodiazepine flumazenil, whose use is controversial following benzodiazepine overdose. Individual benzodiazepines may have different interactions with certain drugs. Depending on their metabolism pathway, benzodiazepines can be divided roughly into two groups. The largest group consists of those that are metabolized by cytochrome P450 (CYP450) enzymes and possess significant potential for interactions with other drugs. The other group comprises those that are metabolized through glucuronidation, such as lorazepam, oxazepam, and temazepam, and, in general, have few drug interactions.[89] Many drugs, including oral contraceptives, some antibiotics, antidepressants, and antifungal agents, inhibit cytochrome enzymes in the liver. They reduce the rate of elimination of the benzodiazepines that are metabolized by CYP450, leading to possibly excessive drug accumulation and increased side-effects. In contrast, drugs that induce cytochrome P450 enzymes, such as St John's wort, the antibiotic rifampicin, and the anticonvulsants carbamazepine and phenytoin, accelerate elimination of many benzodiazepines and decrease their action.[91][179] Taking benzodiazepines with alcohol, opioids and other central nervous system depressants potentiates their action. This often results in increased sedation, impaired motor coordination, suppressed breathing, and other adverse effects that have potential to be lethal.[91][179] Antacids can slow down absorption of some benzodiazepines; however, this effect is marginal and inconsistent.[91] Schematic diagram of the (α1)2(β2)2(γ2) GABAA receptor complex that depicts the five-protein subunits that form the receptor, the chloride (Cl^-) ion channel pore at the center, the two GABA active binding sites at the α1 and β2 interfaces and the benzodiazepine (BZD) allosteric binding site at the α1 and γ2 interface. Benzodiazepines work by increasing the effectiveness of the endogenous chemical, GABA, to decrease the excitability of neurons.[180] This reduces the communication between neurons and, therefore, has a calming effect on many of the functions of the brain. GABA controls the excitability of neurons by binding to the GABAA receptor.[180] The GABAA receptor is a protein complex located in the synapses between neurons. All GABAA receptors contain an ion channel that conducts chloride ions across neuronal cell membranes and two binding sites for the neurotransmitter gamma-aminobutyric acid (GABA), while a subset of GABAA receptor complexes also contain a single binding site for benzodiazepines. Binding of benzodiazepines to this receptor complex does not alter binding of GABA. Unlike other positive allosteric modulators that increase ligand binding, benzodiazepine binding acts as a positive allosteric modulator by increasing the total conduction of chloride ions across the neuronal cell membrane when GABA is already bound to its receptor. This increased chloride ion influx hyperpolarizes the neuron's membrane potential. As a result, the difference between resting potential and threshold potential is increased and firing is less likely. Different GABAA receptor subtypes have varying distributions within different regions of the brain and, therefore, control distinct neuronal circuits. Hence, activation of different GABAA receptor subtypes by benzodiazepines may result in distinct pharmacological actions.[181] In terms of the mechanism of action of benzodiazepines, their similarities are too great to separate them into individual categories such as anxiolytic or hypnotic. For example, a hypnotic administered in low doses produces anxiety-relieving effects, whereas a benzodiazepine marketed as an anti-anxiety drug at higher doses induces sleep.[182] The subset of GABAA receptors that also bind benzodiazepines are referred to as benzodiazepine receptors (BzR). The GABAA receptor is a heteromer composed of five subunits, the most common ones being two αs, two βs, and one γ (α2β2γ1). For each subunit, many subtypes exist (α1–6, β1–3, and γ1–3). GABAA receptors that are made up of different combinations of subunit subtypes have different properties, different distributions in the brain and different activities relative to pharmacological and clinical effects.[183] Benzodiazepines bind at the interface of the α and γ subunits on the GABAA receptor. Binding also requires that alpha subunits contain a histidine amino acid residue, (i.e., α1, α2, α3, and α5 containing GABAA receptors). For this reason, benzodiazepines show no affinity for GABAA receptors containing α4 and α6 subunits with an arginine instead of a histidine residue.[184] Once bound to the benzodiazepine receptor, the benzodiazepine ligand locks the benzodiazepine receptor into a conformation in which it has a greater affinity for the GABA neurotransmitter. This increases the frequency of the opening of the associated chloride ion channel and hyperpolarizes the membrane of the associated neuron. The inhibitory effect of the available GABA is potentiated, leading to sedative and anxiolytic effects. For instance, those ligands with high activity at the α1 are associated with stronger hypnotic effects, whereas those with higher affinity for GABAA receptors containing α2 and/or α3 subunits have good anti-anxiety activity.[185] GABAA receptors participate in the regulation of synaptic pruning by prompting microglial spine engulfment.[186] Benzodiazepines have been shown to upregulate microglial spine engulfment and prompt overzealous eradication of synaptic connections.[187] This mechanism may help explain the increased risk of dementia associated with long-term benzodiazepine treatment.[188] The benzodiazepine class of drugs also interact with peripheral benzodiazepine receptors. Peripheral benzodiazepine receptors are present in peripheral nervous system tissues, glial cells, and to a lesser extent the central nervous system.[189] These peripheral receptors are not structurally related or coupled to GABAA receptors. They modulate the immune system and are involved in the body response to injury.[190][191] Benzodiazepines also function as weak adenosine reuptake inhibitors. It has been suggested that some of their anticonvulsant, anxiolytic, and muscle relaxant effects may be in part mediated by this action.[192] Benzodiazepines have binding sites in the periphery, however their effects on muscle tone is not mediated through these peripheral receptors. The peripheral binding sites for benzodiazepines are present in immune cells and gastrointestinal tract.[8] Benzodiazepine Half-life (range, hours) Speed of onset Alprazolam 6–15[193][194] Intermediate[193] Chlordiazepoxide 10–30[193] Intermediate[193] Clonazepam 19–60[193] Slow[193] Diazepam 20–80[193] Fast[193] Flunitrazepam 18–26 Fast Lorazepam 10–20[193] Intermediate[193] Midazolam 1.5–2.5[195] Fast Oxazepam 5–10[193] Slow[193] Prazepam 50–200[193] Slow[193] Triazolam 1.5 Fast A benzodiazepine can be placed into one of three groups by its elimination half-life, or time it takes for the body to eliminate half of the dose.[196] Some benzodiazepines have long-acting active metabolites, such as diazepam and chlordiazepoxide, which are metabolised into desmethyldiazepam. Desmethyldiazepam has a half-life of 36–200 hours, and flurazepam, with the main active metabolite of desalkylflurazepam, with a half-life of 40–250 hours. These long-acting metabolites are partial agonists.[6][153] Short-acting compounds have a median half-life of 1–12 hours. They have few residual effects if taken before bedtime, rebound insomnia may occur upon discontinuation, and they might cause daytime withdrawal symptoms such as next day rebound anxiety with prolonged usage. Examples are brotizolam, midazolam, and triazolam. Intermediate-acting compounds have a median half-life of 12–40 hours. They may have some residual effects in the first half of the day if used as a hypnotic. Rebound insomnia, however, is more common upon discontinuation of intermediate-acting benzodiazepines than longer-acting benzodiazepines. Examples are alprazolam, estazolam, flunitrazepam, clonazepam, lormetazepam, lorazepam, nitrazepam, and temazepam. Long-acting compounds have a half-life of 40–250 hours. They have a risk of accumulation in the elderly and in individuals with severely impaired liver function, but they have a reduced severity of rebound effects and withdrawal. Examples are diazepam, clorazepate, chlordiazepoxide, and flurazepam. Left: The 1,4-benzodiazepine ring system. Right: 5-phenyl-1H-benzo[e] [1,4]diazepin-2(3H)-one forms the skeleton of many of the most common benzodiazepine pharmaceuticals, such as diazepam (7-chloro-1-methyl substituted). A pharmacophore model of the benzodiazepine binding site on the GABAA receptor.[197] White sticks represent the carbon atoms of the benzodiazepine diazepam, while green represents carbon atoms of the nonbenzodiazepine CGS-9896. Red and blue sticks are oxygen and nitrogen atoms that are present in both structures. The red spheres labeled H1 and H2/A3 are, respectively, hydrogen bond donating and accepting sites in the receptor, while L1, L2, and L3 denote lipophilic binding sites. Benzodiazepines share a similar chemical structure, and their effects in humans are mainly produced by the allosteric modification of a specific kind of neurotransmitter receptor, the GABAA receptor, which increases the overall conductance of these inhibitory channels; this results in the various therapeutic effects as well as adverse effects of benzodiazepines.[180] Other less important modes of action are also known.[190][192] The term benzodiazepine is the chemical name for the heterocyclic ring system (see figure to the right), which is a fusion between the benzene and diazepine ring systems.[198] Under Hantzsch–Widman nomenclature, a diazepine is a heterocycle with two nitrogen atoms, five carbon atom and the maximum possible number of cumulative double bonds. The "benzo" prefix indicates the benzene ring fused onto the diazepine ring.[198] Benzodiazepine drugs are substituted 1,4-benzodiazepines, although the chemical term can refer to many other compounds that do not have useful pharmacological properties. Different benzodiazepine drugs have different side groups attached to this central structure. The different side groups affect the binding of the molecule to the GABAA receptor and so modulate the pharmacological properties.[180] Many of the pharmacologically active "classical" benzodiazepine drugs contain the 5-phenyl-1H-benzo[e] [1,4]diazepin-2(3H)-one substructure (see figure to the right).[199] Benzodiazepines have been found to mimic protein reverse turns structurally, which enable them with their biological activity in many cases.[200][201] Nonbenzodiazepines also bind to the benzodiazepine binding site on the GABAA receptor and possess similar pharmacological properties. While the nonbenzodiazepines are by definition structurally unrelated to the benzodiazepines, both classes of drugs possess a common pharmacophore (see figure to the lower-right), which explains their binding to a common receptor site.[197] Not all benzodiazepines increase the conductance of the GABAA receptor. Flumazenil, an imidazobenzodiazepine, is an antidote for some benzodiazepine overdoses.[202] The structural scaffold can even be used to target receptors other than GABAA.[203] 2-keto compounds: clorazepate, diazepam, flurazepam, halazepam, prazepam, and others[204][205] 3-hydroxy compounds: lorazepam, lormetazepam, oxazepam, temazepam[204][205] 7-nitro compounds: clonazepam, flunitrazepam, nimetazepam, nitrazepam[204][205] Triazolo compounds: adinazolam, alprazolam, estazolam, triazolam[204][205] Imidazo compounds: climazolam, loprazolam, midazolam[204][205] 1,5-benzodiazepines: clobazam The molecular structure of chlordiazepoxide, the first benzodiazepine, marketed by Hoffmann–La Roche beginning in 1960 and branded as Librium The first benzodiazepine, chlordiazepoxide (Librium), was synthesized in 1955 by Leo Sternbach while working at Hoffmann–La Roche on the development of tranquilizers. The pharmacological properties of the compounds prepared initially were disappointing, and Sternbach abandoned the project. Two years later, in April 1957, co-worker Earl Reeder noticed a "nicely crystalline" compound left over from the discontinued project while spring-cleaning in the lab. This compound, later named chlordiazepoxide, had not been tested in 1955 because of Sternbach's focus on other issues. Expecting pharmacology results to be negative, and hoping to publish the chemistry-related findings, researchers submitted it for a standard battery of animal tests. The compound showed very strong sedative, anticonvulsant, and muscle relaxant effects. These impressive clinical findings led to its speedy introduction throughout the world in 1960 under the brand name Librium.[206][207] Following chlordiazepoxide, diazepam marketed by Hoffmann–La Roche under the brand name Valium in 1963, and for a while the two were the most commercially successful drugs. The introduction of benzodiazepines led to a decrease in the prescription of barbiturates, and by the 1970s they had largely replaced the older drugs for sedative and hypnotic uses.[1] The new group of drugs was initially greeted with optimism by the medical profession, but gradually concerns arose; in particular, the risk of dependence became evident in the 1980s. Benzodiazepines have a unique history in that they were responsible for the largest-ever class-action lawsuit against drug manufacturers in the United Kingdom, involving 14,000 patients and 1,800 law firms that alleged the manufacturers knew of the dependence potential but intentionally withheld this information from doctors. At the same time, 117 general practitioners and 50 health authorities were sued by patients to recover damages for the harmful effects of dependence and withdrawal. This led some doctors to require a signed consent form from their patients and to recommend that all patients be adequately warned of the risks of dependence and withdrawal before starting treatment with benzodiazepines.[208] The court case against the drug manufacturers never reached a verdict; legal aid had been withdrawn and there were allegations that the consultant psychiatrists, the expert witnesses, had a conflict of interest.[209][210] The court case fell through, at a cost of £30 million, and led to more cautious funding through legal aid for future cases.[211] This made future class action lawsuits less likely to succeed, due to the high cost from financing a smaller number of cases, and increasing charges for losing the case for each person involved.[210] Although antidepressants with anxiolytic properties have been introduced, and there is increasing awareness of the adverse effects of benzodiazepines, prescriptions for short-term anxiety relief have not significantly dropped.[12] For treatment of insomnia, benzodiazepines are now less popular than nonbenzodiazepines, which include zolpidem, zaleplon and eszopiclone.[212] Nonbenzodiazepines are molecularly distinct, but nonetheless, they work on the same benzodiazepine receptors and produce similar sedative effects.[213] Benzodiazepines have been detected in plant specimens and brain samples of animals not exposed to synthetic sources, including a human brain from the 1940s. However, it is unclear whether these compounds are biosynthesized by microbes or by plants and animals themselves. A microbial biosynthetic pathway has been proposed.[214] In the United States, benzodiazepines are Schedule IV drugs under the Federal Controlled Substances Act, even when not on the market (for example, flunitrazepam[215]), with the exception of flualprazolam, etizolam, clonazolam, flubromazolam, and diclazepam which are placed in Schedule I.[216] In Canada, possession of benzodiazepines is legal for personal use. All benzodiazepines are categorized as Schedule IV substances under the Controlled Drugs and Substances Act.[217] In the United Kingdom, benzodiazepines are Class C controlled drugs, carrying the maximum penalty of 7 years imprisonment, an unlimited fine or both for possession and a maximum penalty of 14 years imprisonment, an unlimited fine or both for supplying benzodiazepines to others.[218][219] In the Netherlands, since October 1993, benzodiazepines, including formulations containing less than 20 mg of temazepam, are all placed on List 2 of the Opium Law. A prescription is needed for possession of all benzodiazepines. Temazepam formulations containing 20 mg or greater of the drug are placed on List 1, thus requiring doctors to write prescriptions in the List 1 format.[220] In East Asia and Southeast Asia, temazepam and nimetazepam are often heavily controlled and restricted. In certain countries, triazolam, flunitrazepam, flutoprazepam and midazolam are also restricted or controlled to certain degrees. In Hong Kong, all benzodiazepines are regulated under Schedule 1 of Hong Kong's Chapter 134 Dangerous Drugs Ordinance.[221] Previously only brotizolam, flunitrazepam and triazolam were classed as dangerous drugs.[222] Internationally, benzodiazepines are categorized as Schedule IV controlled drugs, apart from flunitrazepam, which is a Schedule III drug under the Convention on Psychotropic Substances.[223] Main articles: Benzodiazepine drug misuse and Drug-related crime Xanax (alprazolam) 2 mg tri-score tablets Benzodiazepines are considered major addictive substances.[24] Non-medical benzodiazepine use is mostly limited to individuals who use other substances, i.e., people who engage in polysubstance use.[224] On the international scene, benzodiazepines are categorized as Schedule IV controlled drugs by the INCB, apart from flunitrazepam, which is a Schedule III drug under the Convention on Psychotropic Substances.[225] Some variation in drug scheduling exists in individual countries; for example, in the United Kingdom, midazolam and temazepam are Schedule III controlled drugs.[226] British law requires that temazepam (but not midazolam) be stored in safe custody. Safe custody requirements ensures that pharmacists and doctors holding stock of temazepam must store it in securely fixed double-locked steel safety cabinets and maintain a written register, which must be bound and contain separate entries for temazepam and must be written in ink with no use of correction fluid (although a written register is not required for temazepam in the United Kingdom). Disposal of expired stock must be witnessed by a designated inspector (either a local drug-enforcement police officer or official from health authority).[227][228] Benzodiazepine use ranges from occasional binges on large doses, to chronic and compulsive drug use of high doses.[229] Benzodiazepines are commonly used recreationally by poly-drug users. Mortality is higher among poly-drug users that also use benzodiazepines. Heavy alcohol use also increases mortality among poly-drug users.[22] Polydrug use involving benzodiazepines and alcohol can result in an increased risk of blackouts, risk-taking behaviours, seizures, and overdose.[230] Dependence and tolerance, often coupled with dosage escalation, to benzodiazepines can develop rapidly among people who misuse drugs; withdrawal syndrome may appear after as little as three weeks of continuous use. Long-term use has the potential to cause both physical and psychological dependence and severe withdrawal symptoms such as depression, anxiety (often to the point of panic attacks), and agoraphobia.[17] Benzodiazepines and, in particular, temazepam are sometimes used intravenously, which, if done incorrectly or in an unsterile manner, can lead to medical complications including abscesses, cellulitis, thrombophlebitis, arterial puncture, deep vein thrombosis, and gangrene. Sharing syringes and needles for this purpose also brings up the possibility of transmission of hepatitis, HIV, and other diseases. Benzodiazepines are also misused intranasally, which may have additional health consequences. Once benzodiazepine dependence has been established, a clinician usually converts the patient to an equivalent dose of diazepam before beginning a gradual reduction program.[231] A 1999–2005 Australian police survey of detainees reported preliminary findings that self-reported users of benzodiazepines were less likely than non-user detainees to work full-time and more likely to receive government benefits, use methamphetamine or heroin, and be arrested or imprisoned.[232] Benzodiazepines are sometimes used for criminal purposes; they serve to incapacitate a victim in cases of drug assisted rape or robbery.[233] Overall, anecdotal evidence suggests that temazepam may be the most psychologically habit-forming (addictive) benzodiazepine. Non-medical temazepam use reached epidemic proportions in some parts of the world, in particular, in Europe and Australia, and is a major addictive substance in many Southeast Asian countries. This led authorities of various countries to place temazepam under a more restrictive legal status. Some countries, such as Sweden, banned the drug outright.[234] Temazepam also has certain pharmacokinetic properties of absorption, distribution, elimination, and clearance that make it more apt to non-medical use compared to many other benzodiazepines.[235][236] Benzodiazepines are used in veterinary practice in the treatment of various disorders and conditions. As in humans, they are used in the first-line management of seizures, status epilepticus, and tetanus, and as maintenance therapy in epilepsy (in particular, in cats).[237][238][239] They are widely used in small and large animals (including horses, swine, cattle and exotic and wild animals) for their anxiolytic and sedative effects, as pre-medication before surgery, for induction of anesthesia and as adjuncts to anesthesia.[237][240]

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Portal: Medicine Retrieved from " 2Chemical compound Pharmaceutical compound 2-OxoquazepamIdentifiers IUPAC name 7-Chloro-5-(2-fluorophenyl)-1-(2,2,2-trifluoroethyl)-3H-1,4-benzodiazepin-2-one CAS Number49606-44-2 YPubChem CID93250ChemSpider84187 YUNII8T62S796K7CompTox Dashboard (EPA)DTXSID30197932 ECHA InfoCard100.051.252 Chemical and physical dataFormulaC17H11ClF4N2OMolar mass370.73 g·mol−13D model (JSmol)Interactive image SMILES C1C(=O)N(C2=CC(=C(C=C2)Cl)C(=N1)C3=CC=CC=C3F)CC(F)(F)F InChI InChI=1S/C17H11ClF4N2O/c18-10-5-6-14-12(7-10)16(11-3-1-2-4-13(11)19)23-8-15(25)24(14)9-17(20,21)22/h1-7H,8-9H2 NKey:YFSXBSRGIRSXAD-UHFFFAOYSA-N N NY (what is this?) (verify) 2-Oxoquazepam (Sch 15725) is a benzodiazepine derivative and one of the major active metabolites of quazepam (Doral).[1] ^ Corda MG, Giorgi O, Longoni B, Ongini E, Montaldo S, Biggio G (1988). "Preferential affinity of 3H-2-oxo-quazepam for type I benzodiazepine recognition sites in the human brain". 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