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[Template:Drugbox](/wiki/Template:Drugbox) **Clonazepam**, sold under the brand name **Klonopin** among others, is a medication used to prevent and treat [seizures](/wiki/Seizures), [panic disorder](/wiki/Panic_disorder), and for the [movement disorder](/wiki/Movement_disorder) known as [akathisia](/wiki/Akathisia).<ref name=AHFS2015>[Template:Cite web](/wiki/Template:Cite_web)</ref> It is a tranquilizer of the [benzodiazepine](/wiki/Benzodiazepine) class. It is taken by mouth.<ref name=AHFS2015/> It begins having an effect within an hour and lasts between six and 12 hours.<ref name=Coop2007>[Template:Cite book](/wiki/Template:Cite_book)</ref>

Common side effects include sleepiness, poor coordination, and agitation. It may increase risk of [suicide](/wiki/Suicide). [Long-term use](/wiki/Long-term_effects_of_benzodiazepines) may result in [tolerance](/wiki/Drug_tolerance), [dependence](/wiki/Benzodiazepine_dependence), and [withdrawal symptoms](/wiki/Benzodiazepine_withdrawal_syndrome) if stopped.<ref name=AHFS2015/> Dependence occurs in one-third of people who take clonazepam for longer than four weeks.[[1]](#cite_note-1) If used during pregnancy it may result in harm to the baby.<ref name=AHFS2015/> It binds to GABAA receptors and increases the effect of the neurotransmitter [GABA](/wiki/GABA).[[1]](#cite_note-1) Clonazepam was initially patented in 1964 and went on sale in the United States in 1975.[[2]](#cite_note-2) It is available as a [generic medication](/wiki/Generic_medication).<ref name=AHFS2015/> Wholesale it costs in the [developing world](/wiki/Developing_world) is between 0.01 and 0.07 USD per pill.[[3]](#cite_note-3) In the United States the pills are about 0.40 USD each.<ref name=AHFS2015/> In many areas of the world it is commonly used as a [recreational drug](/wiki/Recreational_drug).[[4]](#cite_note-4)[[5]](#cite_note-5)

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## Medical uses[[edit](/index.php?title=(none)&action=edit&section=1)]

Clonazepam may be prescribed for [epilepsy](/wiki/Epilepsy)[[6]](#cite_note-6)[[7]](#cite_note-7) or [anxiety disorders](/wiki/Anxiety_disorder).

### Seizures[[edit](/index.php?title=(none)&action=edit&section=2)]

Clonazepam, like other benzodiazepines, while being a first-line treatment for acute seizures, is not suitable for the long-term treatment of seizures due to the development of tolerance to the anti-convulsant effects.

Clonazepam has been found effective in treating epilepsy in children, and the inhibition of seizure activity seemed to be achieved at low plasma levels of clonazepam.[[8]](#cite_note-8) As a result, clonazepam is sometimes used for certain rare childhood epilepsies; however, it has been found to be ineffective in the control of infantile spasms.[[9]](#cite_note-9) Clonazepam is mainly prescribed for the acute management of epilepsies. Clonazepam has been found to be effective in the acute control of non-convulsive [status epilepticus](/wiki/Status_epilepticus); however, the benefits tended to be transient in many of the people, and the addition of [phenytoin](/wiki/Phenytoin) for lasting control was required in these patients.[[10]](#cite_note-10) It is also approved for treatment of typical and atypical absences, infantile myoclonic, myoclonic and akinetic seizures[[11]](#cite_note-11) A subgroup of people with treatment resistant epilepsy may benefit from long-term use of clonazepam; the benzodiazepine [clorazepate](/wiki/Clorazepate) may be an alternative due to its slow onset of tolerance.[[1]](#cite_note-1)

### Anxiety disorders[[edit](/index.php?title=(none)&action=edit&section=3)]

Clonazepam has also been found effective in treating:

* [Anxiety disorders](/wiki/Anxiety_disorder), such as [social phobia](/wiki/Social_phobia)[[12]](#cite_note-12)\* [Panic disorder](/wiki/Panic_disorder)[[13]](#cite_note-13)

The effectiveness of clonazepam in the short-term treatment of [panic disorder](/wiki/Panic_disorder) has been demonstrated in [controlled clinical trials](/wiki/Clinical_trial). Some long-term trials have suggested a benefit of clonazepam for up to three years without the development of [tolerance](/wiki/Drug_tolerance) but these trials were not [placebo](/wiki/Placebo)-controlled.[Template:Citation needed](/wiki/Template:Citation_needed) Clonazepam is also effective in the management of [acute mania](/wiki/Acute_mania).[[14]](#cite_note-14)

### Muscle disorders[[edit](/index.php?title=(none)&action=edit&section=4)]

[Restless legs syndrome](/wiki/Restless_legs_syndrome) can be treated using clonazepam as a third-line treatment option as the use of clonazepam is still investigational.[[15]](#cite_note-15)[[16]](#cite_note-16) [Bruxism](/wiki/Bruxism) also responds to clonazepam in the short-term.[[17]](#cite_note-17) [Rapid eye movement behavior disorder](/wiki/Rapid_eye_movement_behavior_disorder) responds well to low doses of clonazepam.[[18]](#cite_note-18)\* The treatment of acute and chronic [akathisia](/wiki/Akathisia) induced by [neuroleptics](/wiki/Neuroleptics), also called [antipsychotics](/wiki/Antipsychotics).[[19]](#cite_note-19)\* [Spasticity](/wiki/Spasticity) related to [amyotrophic lateral sclerosis](/wiki/Amyotrophic_lateral_sclerosis).[[20]](#cite_note-20)\* [Alcohol withdrawal syndrome](/wiki/Alcohol_withdrawal_syndrome)[[21]](#cite_note-21)

### Other[[edit](/index.php?title=(none)&action=edit&section=5)]

* Initial treatment of [mania](/wiki/Mania) or acute psychosis together with first-line drugs such as [lithium](/wiki/Lithium_pharmacology), [haloperidol](/wiki/Haloperidol) or [risperidone](/wiki/Risperidone)[[22]](#cite_note-22)[[23]](#cite_note-23)[Template:Update inline](/wiki/Template:Update_inline)
* [Hyperekplexia](/wiki/Hyperekplexia)[[24]](#cite_note-24)\* Many forms of [parasomnia](/wiki/Parasomnia) and other sleep disorders are treated with clonazepam.[[25]](#cite_note-25)\* It is not effective for preventing [migraines](/wiki/Migraines).[[26]](#cite_note-26)

## Adverse effects[[edit](/index.php?title=(none)&action=edit&section=6)]

[Template:Confusing section](/wiki/Template:Confusing_section)

### Common[[edit](/index.php?title=(none)&action=edit&section=7)]

* [Drowsiness](/wiki/Drowsiness), Sedation[[27]](#cite_note-27)\* [Motor impairment](/wiki/Psychomotor_retardation)

### Less common[[edit](/index.php?title=(none)&action=edit&section=8)]

* [Confusion](/wiki/Confusion)[[1]](#cite_note-1)\* Irritability and aggression[[28]](#cite_note-28)\* [Psychomotor agitation](/wiki/Psychomotor_agitation)[[29]](#cite_note-29)\* Lack of motivation[[30]](#cite_note-30)\* Loss of libido
* Impaired motor function[Template:Vague](/wiki/Template:Vague)
  + Impaired coordination
  + Impaired balance
  + Dizziness
* Cognitive impairments[Template:Vague](/wiki/Template:Vague)[[31]](#cite_note-31)\*\* [Hallucinations](/wiki/Hallucinations)[[32]](#cite_note-32)\*\* Short-term memory loss[[33]](#cite_note-33)\*\* [Anterograde amnesia](/wiki/Anterograde_amnesia) (common with higher doses)[[34]](#cite_note-34)\* Some users report [hangover](/wiki/Hangover)-like symptoms of drowsiness, headaches, sluggishness, and irritability upon waking up if the medication was taken before sleep. This is likely the result of the medication's long half-life, which continues to affect the user after waking up.[Template:Citation needed](/wiki/Template:Citation_needed)

[[35]](#cite_note-35)[[36]](#cite_note-36) While benzodiazepines induce sleep, they tend to reduce the quality of sleep by suppressing or disrupting REM sleep.[[37]](#cite_note-37) After regular use, [rebound insomnia](/wiki/Rebound_insomnia) may occur when discontinuing clonazepam.[[38]](#cite_note-38)\* Benzodiazepines may cause or worsen [depression](/wiki/Major_depression).[[1]](#cite_note-1)

### Occasional[[edit](/index.php?title=(none)&action=edit&section=9)]

* [Dysphoria](/wiki/Dysphoria)[[39]](#cite_note-39)\* [Thrombocytopenia](/wiki/Thrombocytopenia)[[40]](#cite_note-40)\* Induction of seizures[[41]](#cite_note-41)[[42]](#cite_note-42) or increased frequency of seizures[[43]](#cite_note-43)\* Personality changes[[44]](#cite_note-44)\* Behavioural disturbances[[45]](#cite_note-45)\* [Ataxia](/wiki/Ataxia)[[1]](#cite_note-1)

### Rare[[edit](/index.php?title=(none)&action=edit&section=10)]

* [Psychosis](/wiki/Psychosis)[[46]](#cite_note-46)\* [Incontinence](/wiki/Urinary_incontinence)[[47]](#cite_note-47)[[48]](#cite_note-48)[[49]](#cite_note-49)\* Liver damage[[50]](#cite_note-50)\* Paradoxical behavioural disinhibition[[1]](#cite_note-1)[[51]](#cite_note-51) (most frequently in children, the elderly, and in persons with developmental disabilities)
  + Rage
  + Excitement
  + Impulsivity

The [long-term effects of clonazepam](/wiki/Long-term_effects_of_benzodiazepines) can include [depression](/wiki/Major_depression),[[1]](#cite_note-1) [disinhibition](/wiki/Disinhibition), and [sexual dysfunction](/wiki/Sexual_dysfunction).[[52]](#cite_note-52)

### Drowsiness[[edit](/index.php?title=(none)&action=edit&section=11)]

Clonazepam, like other benzodiazepines, may impair a person's ability to drive or operate machinery. The central nervous system-depressing effects of the drug can be intensified by alcohol consumption, and therefore alcohol should be avoided while taking this medication. Benzodiazepines have been shown to cause dependence. Patients dependent on clonazepam should be slowly titrated off under the supervision of a qualified healthcare professional to reduce the intensity of withdrawal or rebound symptoms.

### Withdrawal-related[[edit](/index.php?title=(none)&action=edit&section=12)]

* Anxiety, irritability, insomnia, tremors
* Potential to exacerbate existing panic disorder upon discontinuation
* Seizures[[53]](#cite_note-53) similar to [delirium tremens](/wiki/Delirium_tremens) (with long-term use of excessive doses)

Benzodiazepines such as clonazepam can be very effective in controlling [status epilepticus](/wiki/Status_epilepticus), but, when used for longer periods of time, some potentially serious side-effects may develop, such as interference with [cognitive](/wiki/Cognitive) functions and behavior.[[54]](#cite_note-54) Many individuals treated on a long-term basis develop a form of dependence known as "low-dose dependence", as was shown in one double-blind, placebo-controlled study of 34 [therapeutic](/wiki/Pharmacotherapy) low-dose benzodiazepine users.[Template:Citation needed](/wiki/Template:Citation_needed) [Physiological](/wiki/Physiological) dependence was demonstrated by [flumazenil](/wiki/Flumazenil)-precipitated withdrawal.[[55]](#cite_note-55)Use of alcohol or other [CNS](/wiki/Central_nervous_system) depressants while taking clonazepam greatly intensifies the effects (and side-effects) of the drug.

### Tolerance and withdrawal[[edit](/index.php?title=(none)&action=edit&section=13)]

[Template:Main article](/wiki/Template:Main_article) Like all benzodiazepines, clonazepam is a GABA positive [allosteric modulator](/wiki/Allosteric_modulator).[[56]](#cite_note-56)[[57]](#cite_note-57) One-third of individuals treated with benzodiazepines for longer than four weeks develop a dependence on the drug and experience a withdrawal syndrome upon dose reduction. High dosage and long-term use increases the risk and severity of dependence and withdrawal symptoms. Withdrawal seizures and psychosis can occur in severe cases of withdrawal, and anxiety and insomnia can occur in less severe cases of withdrawal. Gradual reduction in dosage reduces the severity of the [benzodiazepine withdrawal syndrome](/wiki/Benzodiazepine_withdrawal_syndrome). Due to the risks of tolerance and withdrawal seizures, clonazepam is generally not recommended for the long-term management of epilepsies. Increasing the dose can overcome the effects of tolerance, but tolerance to the higher dose may occur and adverse effects may intensify. The mechanism of tolerance includes receptor desensitisation, down regulation, receptor decoupling, and alterations in subunit composition and in [gene transcription](/wiki/Gene_transcription) coding.[[1]](#cite_note-1) [Tolerance](/wiki/Drug_tolerance) to the anticonvulsant effects of clonazepam occurs in both animals and humans. In humans, tolerance to the anticonvulsant effects of clonazepam occurs frequently.[[58]](#cite_note-58)[[59]](#cite_note-59) Chronic use of benzodiazepines can lead to the development of tolerance with a decrease of benzodiazepine binding sites. The degree of tolerance is more pronounced with clonazepam than with [chlordiazepoxide](/wiki/Chlordiazepoxide).[[60]](#cite_note-60) In general, short-term therapy is more effective than long-term therapy with clonazepam for the treatment of epilepsy.[[61]](#cite_note-61) Many studies have found that tolerance develops to the anticonvulsant properties of clonazepam with chronic use, which limits its long-term effectiveness as an anticonvulsant.[[62]](#cite_note-62) Abrupt or over-rapid withdrawal from clonazepam may result in the development of the benzodiazepine withdrawal syndrome, causing psychosis characterised by [dysphoric](/wiki/Dysphoric) manifestations, irritability, aggressiveness, anxiety, and hallucinations.[[63]](#cite_note-63)[[64]](#cite_note-64)[[65]](#cite_note-65) Sudden withdrawal may also induce the potentially life-threatening condition, [status epilepticus](/wiki/Status_epilepticus). Anti-epileptic drugs, benzodiazepines such as clonazepam in particular, should be reduced in dose slowly and gradually when discontinuing the drug to mitigate withdrawal effects.[[44]](#cite_note-44) [Carbamazepine](/wiki/Carbamazepine) has been tested in the treatment of clonazepam withdrawal but was found to be ineffective in preventing clonazepam withdrawal-induced [status epilepticus](/wiki/Status_epilepticus) from occurring.[[66]](#cite_note-66)

### Overdose[[edit](/index.php?title=(none)&action=edit&section=14)]

[Template:Main article](/wiki/Template:Main_article) Excess doses may result in:

* [difficulty staying awake](/wiki/Somnolence)
* Mental confusion
* [Nausea](/wiki/Nausea)
* Impaired motor functions
  + Impaired reflexes
  + Impaired coordination
  + Impaired balance
  + Dizziness
* Respiratory depression
* [Hypotension](/wiki/Hypotension)
* [Coma](/wiki/Coma)

Coma can be cyclic, with the individual alternating from a comatose state to a hyper-alert state of consciousness, which occurred in a 4-year-old boy who suffered an overdose of clonazepam.[[67]](#cite_note-67) The combination of clonazepam and certain barbiturates, e.g. [amobarbital](/wiki/Amobarbital), at prescribed doses has resulted in a [synergistic](/wiki/Synergistic) potentiation of the effects of each drug, leading to serious respiratory depression.[[68]](#cite_note-68) Overdose symptoms may include extreme drowsiness, confusion, muscle weakness, and fainting.[[69]](#cite_note-69) Although an overdose of clonazepam is a serious medical concern, there have been no known instances of death from such an overdose. The [LD50](/wiki/LD50) for both mice and rats is greater than 2,000 mg per kilogram of body weight.[[70]](#cite_note-70)

### Detection in biological fluids[[edit](/index.php?title=(none)&action=edit&section=15)]

Clonazepam and 7-aminoclonazepam may be quantified in [plasma](/wiki/Blood_plasma), [serum](/wiki/Serum_(blood)) or [whole blood](/wiki/Whole_blood) in order to monitor compliance in those receiving the drug therapeutically. Results from such tests can be used to confirm the diagnosis in potential poisoning victims or to assist in the forensic investigation in a case of fatal overdosage. Both the parent drug and 7-aminoclonazepam are unstable in biofluids, and therefore specimens should be preserved with sodium fluoride, stored at the lowest possible temperature and analyzed quickly to minimize losses.[[71]](#cite_note-71)

### Special precautions[[edit](/index.php?title=(none)&action=edit&section=16)]

The elderly metabolise benzodiazepines more slowly than younger individuals and are also more sensitive to the effects of benzodiazepines, even at similar blood plasma levels. Doses for the elderly are recommended to be about half of that given to younger adults and are to be administered for no longer than two weeks. Long-acting benzodiazepines such as clonazepam are not generally recommended for the elderly due the risk of drug accumulation.[[1]](#cite_note-1) The elderly are especially susceptible to increased risk of harm from motor impairments and drug accumulation side effects. Benzodiazepines also require special precaution if used by individuals that may be pregnant, alcohol- or drug-dependent, or may have [comorbid](/wiki/Comorbid) [psychiatric disorders](/wiki/Psychiatric_disorders).[[72]](#cite_note-72) Clonazepam is generally not recommended for use in elderly people for insomnia due to its high potency relative to other benzodiazepines.[[73]](#cite_note-73) Clonazepam is not recommended for use in those under 18. Use in very young children may be especially hazardous. Of anticonvulsant drugs, behavioural disturbances occur most frequently with clonazepam and [phenobarbital](/wiki/Phenobarbital).[[72]](#cite_note-72)[[74]](#cite_note-74) Doses higher than 0.5–1 mg per day are associated with significant sedation.[[75]](#cite_note-75) Clonazepam may aggravate [hepatic porphyria](/wiki/Hepatic_porphyria).[[76]](#cite_note-76)[[77]](#cite_note-77) Clonazepam is not recommended for patients with chronic [schizophrenia](/wiki/Schizophrenia). A 1982 double-blinded, placebo-controlled study found clonazepam increases violent behavior in individuals with chronic schizophrenia.[[78]](#cite_note-78)

## Interactions[[edit](/index.php?title=(none)&action=edit&section=17)]

Clonazepam decreases the levels of [carbamazepine](/wiki/Carbamazepine),[[79]](#cite_note-79)[[80]](#cite_note-80) and, likewise, clonazepam's level is reduced by carbamazepine. Azole antifungals, such as [ketoconazole](/wiki/Ketoconazole), may inhibit the metabolism of clonazepam.[[1]](#cite_note-1) Clonazepam may affect levels of [phenytoin](/wiki/Phenytoin) (diphenylhydantoin).[[79]](#cite_note-79)[[81]](#cite_note-81)[[82]](#cite_note-82)[[83]](#cite_note-83) In turn, Phenytoin may lower clonazepam plasma levels by increasing the speed of clonazepam clearance by approximately 50% and decreasing its half-life by 31%.[[84]](#cite_note-84)Clonazepam increases the levels of [primidone](/wiki/Primidone)[[82]](#cite_note-82) and [phenobarbital](/wiki/Phenobarbital).[[85]](#cite_note-85) Combined use of clonazepam with certain [antidepressants](/wiki/Antidepressants), [antiepileptics](/wiki/Antiepileptics), such as [phenobarbital](/wiki/Phenobarbital), [phenytoin](/wiki/Phenytoin) and [carbamazepine](/wiki/Carbamazepine), sedative [antihistamines](/wiki/Antihistamines), [opiates](/wiki/Opiates), [antipsychotics](/wiki/Antipsychotics), [nonbenzodiazepine](/wiki/Nonbenzodiazepine) hypnotics like [zolpidem](/wiki/Zolpidem) and alcohol may result in enhanced sedative effects.[[1]](#cite_note-1)

## Pregnancy[[edit](/index.php?title=(none)&action=edit&section=18)]

[Template:See also](/wiki/Template:See_also) There is some medical evidence of various malformations, e.g., cardiac or facial deformations, when used in early pregnancy; however, the data is not conclusive. The data are also inconclusive on whether benzodiazepines such as clonazepam cause developmental deficits or decreases in IQ in the developing fetus when taken by the mother during pregnancy. Clonazepam, when used late in pregnancy, may result in the development of a severe benzodiazepine withdrawal syndrome in the [neonate](/wiki/Neonate). Withdrawal symptoms from benzodiazepines in the [neonate](/wiki/Neonate) may include [hypotonia](/wiki/Hypotonia), [apnoeic](/wiki/Apnoeic) spells, [cyanosis](/wiki/Cyanosis) and impaired [metabolic](/wiki/Metabolic) responses to cold stress.[[86]](#cite_note-86) The safety profile of clonazepam during pregnancy is less clear than that of other benzodiazepines, and if benzodiazepines are indicated during pregnancy, [chlordiazepoxide](/wiki/Chlordiazepoxide) and [diazepam](/wiki/Diazepam) may be a safer choice. The use of clonazepam during pregnancy should only occur if the clinical benefits are believed to outweigh the clinical risks to the [fetus](/wiki/Fetus). Caution is also required if clonazepam is used during breast feeding. Possible adverse effects of use of benzodiazepines such as clonazepam during pregnancy include: [miscarriage](/wiki/Miscarriage), [malformation](/wiki/Malformation), [intrauterine growth retardation](/wiki/Intrauterine_growth_retardation), functional deficits, [floppy infant syndrome](/wiki/Floppy_infant_syndrome), [carcinogenesis](/wiki/Carcinogenesis) and [mutagenesis](/wiki/Mutagenesis). Neonatal withdrawal syndrome associated with benzodiazepines include [hypertonia](/wiki/Hypertonia), [hyperreflexia](/wiki/Hyperreflexia), [restlessness](/wiki/Anxiety), [irritability](/wiki/Irritability), abnormal sleep patterns, inconsolable crying, [tremors](/wiki/Tremors) or jerking of the extremities, [bradycardia](/wiki/Bradycardia), [cyanosis](/wiki/Cyanosis), [suckling](/wiki/Suckling) difficulties, [apnea](/wiki/Apnea), risk of aspiration of feeds, [diarrhea](/wiki/Diarrhea) and vomiting, and [growth retardation](/wiki/Growth_retardation). This syndrome can develop between 3 days to 3 weeks after birth and can have a duration of up to several months. The pathway by which clonazepam is metabolised is usually impaired in newborns. If clonazepam is used during pregnancy or [breast feeding](/wiki/Breast_feeding), it is recommended that serum levels of clonazepam are monitored and that signs of [central nervous system](/wiki/Central_nervous_system) depression and [apnea](/wiki/Apnea) are also checked for. In many cases, non-pharmacological treatments, such as relaxation therapy, psychotherapy and avoidance of [caffeine](/wiki/Caffeine), can be an effective and safer alternative to the use of benzodiazepines for anxiety in pregnant women.[[87]](#cite_note-87)

## Mechanism of action[[edit](/index.php?title=(none)&action=edit&section=19)]

Clonazepam acts by binding to the benzodiazepine site of the GABA receptors, which enhances the electric effect of GABA binding on neurons, resulting in an increased influx of chloride ions into the neurons. This further results in an inhibition of synaptic transmission across the [central nervous system](/wiki/Central_nervous_system).[[88]](#cite_note-88)[[89]](#cite_note-89) Benzodiazepines do not have any effect on the levels of GABA in the brain.[[90]](#cite_note-90) Clonazepam has no effect on GABA levels and has no effect on gamma-aminobutyric acid transaminase. Clonazepam does, however, affect [glutamate decarboxylase](/wiki/Glutamate_decarboxylase) activity. It differs from other anticonvulsant drugs it was compared to in a study.[[91]](#cite_note-91) Clonazepam's primary [mechanism of action](/wiki/Mechanism_of_action) is the modulation of [GABA](/wiki/GABA) function in the brain, by the benzodiazepine receptor, located on [GABAA receptors](/wiki/GABAA_receptor), which, in turn, leads to enhanced GABAergic inhibition of neuronal firing. Benzodiazepines do not replace GABA, but instead enhance the effect of GABA at the GABAA receptor by increasing the opening frequency of chloride ion channels, which leads to an increase in GABA's inhibitory effects and resultant central nervous system depression.[[1]](#cite_note-1) In addition, clonazepam decreases the utilization of [5-HT (serotonin)](/wiki/Serotonin) by neurons[[92]](#cite_note-92)[[93]](#cite_note-93) and has been shown to bind tightly to central-type benzodiazepine receptors.[[94]](#cite_note-94) Because clonazepam is effective in low milligram doses (0.5 mg clonazepam = 10 mg diazepam),[[95]](#cite_note-95) it is said to be among the class of "highly potent" [benzodiazepines](/wiki/Benzodiazepines).[[96]](#cite_note-96) The anticonvulsant properties of benzodiazepines are due to the enhancement of [synaptic](/wiki/Synapse) GABA responses, and the inhibition of sustained, high-frequency repetitive firing.[[97]](#cite_note-97) Benzodiazepines, including clonazepam, bind to mouse [glial cell](/wiki/Glial_cell) membranes with high affinity.[[98]](#cite_note-98)[[99]](#cite_note-99) Clonazepam decreases release of [acetylcholine](/wiki/Acetylcholine) in the feline brain[[100]](#cite_note-100) and decreases [prolactin](/wiki/Prolactin) release in rats.[[101]](#cite_note-101) Benzodiazepines inhibit cold-induced [thyroid stimulating hormone](/wiki/Thyroid_stimulating_hormone) (also known as TSH or thyrotropin) release.[[102]](#cite_note-102) Benzodiazepines acted via [micromolar](/wiki/Micromolar) benzodiazepine binding sites as [Ca2+ channel blockers](/wiki/Calcium_channel_blocker) and significantly inhibit depolarization-sensitive calcium uptake in experimentation on rat brain cell components. This has been conjectured as a mechanism for high-dose effects on seizures in the study.[[103]](#cite_note-103) Clonazepam is a [chlorinated](/wiki/Halogenation) derivative of [nitrazepam](/wiki/Nitrazepam)[[104]](#cite_note-104) and therefore a chloro-nitrobenzodiazepine.[[105]](#cite_note-105)

## Pharmacokinetics[[edit](/index.php?title=(none)&action=edit&section=20)]

Clonazepam is lipid-soluble, rapidly crosses the [blood–brain barrier](/wiki/Blood–brain_barrier), and penetrates the placenta. It is extensively metabolised into pharmacologically inactive metabolites. Clonazepam is metabolized extensively via nitroreduction by [cytochrome P450](/wiki/Cytochrome_P450) enzymes, particularly [CYP2C19](/wiki/CYP2C19) and to a lesser extent [CYP3A4](/wiki/CYP3A4). [Erythromycin](/wiki/Erythromycin), [clarithromycin](/wiki/Clarithromycin), [ritonavir](/wiki/Ritonavir), [itraconazole](/wiki/Itraconazole), [ketoconazole](/wiki/Ketoconazole), [nefazodone](/wiki/Nefazodone), and grapefruit juice are inhibitors of CYP3A4 and can affect the metabolism of benzodiazepines.[[106]](#cite_note-106)It has an [elimination half-life](/wiki/Elimination_half-life) of 19–60 hours.[[1]](#cite_note-1) Peak blood concentrations of 6.5–13.5 ng/mL were usually reached within 1–2 hours following a single 2 mg oral dose of micronized clonazepam in healthy adults. In some individuals, however, peak blood concentrations were reached at 4–8 hours.[[107]](#cite_note-107) Clonazepam passes rapidly into the central nervous system, with levels in the brain corresponding with levels of unbound clonazepam in the blood serum.[[108]](#cite_note-108) Clonazepam plasma levels are very unreliable amongst patients. Plasma levels of clonazepam can vary as much as tenfold between different patients.[[109]](#cite_note-109) Clonazepam is largely bound to plasma proteins.[[110]](#cite_note-110) Clonazepam passes through the blood–brain barrier easily, with blood and brain levels corresponding equally with each other.[[111]](#cite_note-111) The metabolites of clonazepam include 7-aminoclonazepam, 7-acetaminoclonazepam and 3-hydroxy clonazepam.[[112]](#cite_note-112)[[113]](#cite_note-113)

## Society and culture[[edit](/index.php?title=(none)&action=edit&section=21)]

### Recreational use[[edit](/index.php?title=(none)&action=edit&section=22)]

[Template:See also](/wiki/Template:See_also) A 2006 US government study of emergency department visits found that sedative-hypnotics were the most frequently implicated pharmaceutical drug in ED visits, with benzodiazepines accounting for the majority of these. Clonazepam was the second most frequently implicated benzodiazepine in ED visits, however it should be noted that alcohol alone was responsible for over twice as many ED visits than clonazepam in the same study. The study examined the number of times non-medical use of certain drugs were implicated in ED visit. The criteria for non-medical use in this study were purposefully broad, and include, for example, [drug abuse](/wiki/Drug_abuse), accidental or intentional [overdose](/wiki/Overdose), or adverse reactions resulting from legitimate use of the medication.<ref name=dawn2neodredv>[Template:Cite web](/wiki/Template:Cite_web)</ref>

### Formulations[[edit](/index.php?title=(none)&action=edit&section=23)]

Clonazepam was approved in the United States as a [generic drug](/wiki/Generic_drug) in 1997 and is now manufactured and marketed by several companies.

Clonazepam is available as tablets (0.25 mg, 0.5 mg, 1.0 mg, 2.0 mg) and orally disintegrating tablets (wafers) (0.25 mg, 0.5 mg), an oral solution (drops), and as a solution for injection or intravenous infusion.[Template:Citation needed](/wiki/Template:Citation_needed)

### Brand names[[edit](/index.php?title=(none)&action=edit&section=24)]

It is marketed under the trade name Rivotril by [Roche](/wiki/Hoffmann-La_Roche) in Argentina, Australia, Austria, Belgium, Brazil, Bulgaria, Canada, Colombia, Costa Rica, Croatia, the Czech Republic, Denmark, Germany, Hungary, Ireland, Italy, China, the Netherlands, Norway, Portugal, Peru, Romania, South Africa, Spain, Turkey, and the United States; Linotril and Clonotril in India, South Korea, and other parts of Europe; and under the trade name Klonopin by [Roche](/wiki/Hoffmann-La_Roche) in the United States. Other names, such as Clonoten, Ravotril, Rivatril, Rivotril, Iktorivil, Clonex, Paxam, Petril, Naze and Kriadex, are known throughout the world.[Template:Citation needed](/wiki/Template:Citation_needed)

<gallery> Image:klonopin0.5mg.jpg|Klonopin 0.5 mg Image:klonopin1mg.jpg|Klonopin 1 mg File:Clonazepam 2MG.jpg|Klonopin 2 mg </gallery> [Template:Clear](/wiki/Template:Clear)

## References[[edit](/index.php?title=(none)&action=edit&section=25)]

[Template:Research help](/wiki/Template:Research_help) [Template:Reflist](/wiki/Template:Reflist)

## External links[[edit](/index.php?title=(none)&action=edit&section=26)]

[Template:Commons category](/wiki/Template:Commons_category)

* [Rx-List - Clonazepam](http://www.rxlist.com/cgi/generic/clonaz.htm)
* [Poisons Information Monograph - Clonazepam](http://www.inchem.org/documents/pims/pharm/pim326.htm)
* [FDA prescription insert](http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/017533s045,020813s005lbl.pdf)

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[Category:Chloroarenes](/wiki/Category:Chloroarenes) [Category:GABAA receptor positive allosteric modulators](/wiki/Category:GABAA_receptor_positive_allosteric_modulators) [Category:Glycine receptor antagonists](/wiki/Category:Glycine_receptor_antagonists) [Category:Hoffmann-La Roche](/wiki/Category:Hoffmann-La_Roche) [Category:Lactams](/wiki/Category:Lactams) [Category:Nitrobenzodiazepines](/wiki/Category:Nitrobenzodiazepines) [Category:RTT](/wiki/Category:RTT)