[Template:Use dmy dates](/wiki/Template:Use_dmy_dates" \o "Template:Use dmy dates) [Template:Drugbox](/wiki/Template:Drugbox)

**Tramadol**, sold under the brandname **Tramal** among others,<ref name=generics/> is an [opioid](/wiki/Opioid) [pain medication](/wiki/Analgesic) used to treat moderate to moderately severe [pain](/wiki/Pain).<ref name=AHFS2014>[Template:Cite web](/wiki/Template:Cite_web)</ref> When taken as an immediate-release oral formulation, the onset of pain relief usually occurs within about an hour.[[1]](#cite_note-1) It has two different mechanisms. First, it binds to the [μ-opioid receptor](/wiki/Μ-opioid_receptor). Second, it inhibits the [reuptake](/wiki/Reuptake) of [serotonin](/wiki/Serotonin) and [norepinephrine](/wiki/Norepinephrine).[[2]](#cite_note-2)<ref name = phr09/>

Serious side effects may include [seizures](/wiki/Seizure), increased risk of [serotonin syndrome](/wiki/Serotonin_syndrome), decreased alertness, and [drug addiction](/wiki/Drug_addiction).<ref name=AHFS2014/>, although the risk of serotonin syndrome appears to be low.[[3]](#cite_note-3) Common side effects include: [constipation](/wiki/Constipation), [itchiness](/wiki/Puritis) and nausea, among others. A change in dosage may be recommended in those with kidney or liver problems. Its use is not recommended in women who are [breastfeeding](/wiki/Breastfeeding) or those who are at risk of [suicide](/wiki/Suicide).<ref name=AHFS2014/>

Tramadol is marketed as a [racemic mixture](/wiki/Racemic_mixture) of both *R*- and *S*-[stereoisomers](/wiki/Stereoisomers).<ref name = MD/> This is because the two isomers complement each other's analgesic activity.<ref name = MD/> It is often combined with [paracetamol](/wiki/Paracetamol) (acetaminophen) as this is known to improve the efficacy of tramadol in relieving pain.<ref name = MD/> Tramadol is metabolised to [*O*-desmethyltramadol](/wiki/O-Desmethyltramadol), which is a more potent opioid.[[4]](#cite_note-4) It is of the benzenoid class.

Tramadol was launched and marketed as "Tramal" by the German [pharmaceutical company](/wiki/Pharmaceutical_company) [Grünenthal GmbH](/wiki/Grünenthal) in 1977 in [West Germany](/wiki/West_Germany), and 20 years later it was launched in countries such as the UK, US, and Australia.<ref name = phr09>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> It is marketed under many brand names worldwide.<ref name=generics>Drugs.com [International names for tramadol](http://www.drugs.com/international/tramadol.html) Page accessed April 23, 2016</ref>

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

[thumb|Generic tramadol HCl tablets marketed by Amneal Pharmaceuticals.](/wiki/File:50_mg_Tramadol_HCl_tablets_(generic_Ultram)_marketed_by_Amneal_Pharmaceuticals_(rotated).jpg) [thumb|Tramadol HCl for injection](/wiki/File:Tramadol_HCl.jpg)

Tramadol is used primarily to treat mild–severe pain, both acute and chronic.[[5]](#cite_note-5) Its analgesic effects take about one hour to come into effect and 2–4 hours to peak after oral administration with an immediate-release formulation.<ref name = AMH/> On a dose-by-dose basis tramadol has about one-tenth the potency of [morphine](/wiki/Morphine) and is approximately equally potent when compared to [pethidine](/wiki/Pethidine) and [codeine](/wiki/Codeine).[[6]](#cite_note-6) For pain moderate in severity its effectiveness is equivalent to that of morphine; for severe pain it is less effective than morphine.<ref name = AMH/> These painkilling effects peak at about 3 hours, post-oral administration and last for approximately 6 hours.<ref name = Grond\_Sablotzki\_2004/>

Available dosage forms include liquids, syrups, drops, elixirs, effervescent tablets and powders for mixing with water, capsules, tablets including extended release formulations, suppositories, compounding powder, and injections.<ref name = AMH/>

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

Tramadol's use in [pregnancy](/wiki/Pregnancy) is generally avoided as it may cause some reversible withdrawal effects in the newborn.[[7]](#cite_note-7) A small prospective study in France found that, while there was an increased risk of [miscarriages](/wiki/Miscarriages), there were no major malformations reported in the newborn.<ref name = pregrev/> Its use during [lactation](/wiki/Lactation) is also generally advised against, but a small trial found that infants breastfed by mothers taking tramadol were exposed to about 2.88% of the dose the mothers were taking. There was no evidence of this dose having a harmful effect on the newborn.<ref name = pregrev/>

### Labour and delivery[[edit](/index.php?title=(none)&action=edit&section=3)]

Its use as an analgesic during labour is generally advised against due to its long-onset of action (one hour).<ref name = pregrev/> The ratio of the mean concentration of the drug in the fetus compared to that of the mother when it is given intramuscularly for labour pains has been estimated to be 94.<ref name = pregrev/>

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

Its use in children is generally advised against, although it may be done under the supervision of a specialist.<ref name = AMH/> On September 21, 2015 the FDA started investigating the safety of tramadol in use in persons under the age of 17. The investigation was initiated because some of these people have experienced slowed or difficult breathing.[[8]](#cite_note-8)

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

There is an increased risk of opioid-related adverse effects such as [respiratory depression](/wiki/Hypoventilation), falls, cognitive impairment and sedation.<ref name = AMH/>

### Liver and kidney failure[[edit](/index.php?title=(none)&action=edit&section=6)]

It is advised that the drug be used with caution in those with liver or kidney failure, due to the high dependence of the drug on the liver and kidneys for metabolism to [O-desmethyltramadol](/wiki/O-desmethyltramadol) and elimination, respectively.<ref name = AMH/>

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

[Template:Main](/wiki/Template:Main) [thumb|280px|right|Main side effects of tramadol. Red color denotes more serious effects, requiring immediate contact with health provider.](/wiki/File:Side_effects_of_Tramadol.png)[[9]](#cite_note-9)

The most common [adverse effects](/wiki/Adverse_effect) of tramadol include [nausea](/wiki/Nausea), [dizziness](/wiki/Dizziness), [dry mouth](/wiki/Xerostomia), [indigestion](/wiki/Indigestion), abdominal pain, [vertigo](/wiki/Vertigo), [vomiting](/wiki/Vomiting), [constipation](/wiki/Constipation), drowsiness and [headache](/wiki/Headache).<ref name = AEP>[Template:Cite journal](/wiki/Template:Cite_journal)</ref><ref name = drugs06>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> Compared to other opioids, [respiratory depression](/wiki/Hypoventilation) and constipation are considered less of a problem with tramadol.<ref name = drugs06/>

There are suggestions that chronic opioid administration may induce a state of [immune tolerance](/wiki/Immune_tolerance),[[10]](#cite_note-10) although tramadol, in contrast to typical opioids, may enhance immune function.[[11]](#cite_note-11)[[12]](#cite_note-12)[[13]](#cite_note-13) Some have also stressed the negative effects of opioids on cognitive functioning and personality.[[14]](#cite_note-14)

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

Tramadol may interact with [serotonergics](/wiki/Antidepressants), [monoamine oxidase inhibitors](/wiki/Monoamine_oxidase_inhibitors), [tricyclic antidepressants](/wiki/Tricyclic_antidepressants), [selective serotonin reuptake inhibitors](/wiki/Selective_serotonin_reuptake_inhibitors), [serotonin-norepinephrine reuptake inhibitors](/wiki/Serotonin-norepinephrine_reuptake_inhibitors), [noradrenergic and specific serotonergic antidepressants](/wiki/Noradrenergic_and_specific_serotonergic_antidepressants), [serotonin antagonists and reuptake inhibitors](/wiki/Serotonin_antagonist_and_reuptake_inhibitors), other opioid [analgesics](/wiki/Analgesics) ([pethidine](/wiki/Pethidine) (meperidine), [tapentadol](/wiki/Tapentadol), [oxycodone](/wiki/Oxycodone), and [fentanyl](/wiki/Fentanyl)), [dextromethorphan](/wiki/Dextromethorphan), certain migraine medications ([triptans](/wiki/Triptan), [ergots](/wiki/Ergoline)), certain [anxiolytics](/wiki/Anxiolytics) (such as the [SSRIs](/wiki/SSRI) and [buspirone](/wiki/Buspirone)), certain [antibiotics](/wiki/Antibiotics) (namely, [linezolid](/wiki/Linezolid) and [isoniazid](/wiki/Isoniazid)), certain herbs (e.g. [St. John's wort](/wiki/St._John's_wort), [passiflora](/wiki/Passiflora), etc.), [amphetamines](/wiki/Amphetamine), substituted amphetamines, [phenethylamine](/wiki/Phenethylamine) and [substituted phenethylamines](/wiki/Substituted_phenethylamine), [phentermine](/wiki/Phentermine), [lithium](/wiki/Lithium), [methylene blue](/wiki/Methylene_blue) as well as numerous other therapeutic agents.[[15]](#cite_note-15)[[16]](#cite_note-16) As it is a substrate of [CYP3A4](/wiki/CYP3A4) and [CYP2D6](/wiki/CYP2D6), any agents with the ability to inhibit or induce these enzymes will likely interact with tramadol. A [pressor](/wiki/Antihypotensive_agent) response similar to the so-called "[cheese effect](/wiki/Tyramine#Physical_effects_and_pharmacology)" was noted in combinations of amphetamine and tramadol, which appears to cause dysfunction of or toxicity to [epinephrine/norepinephrine receptors](/wiki/Adrenergic_receptor).<ref name = AMH/><ref name = drugs06/> [Cyclobenzaprine](/wiki/Cyclobenzaprine), a commonly-used muscle relaxant, atypical analgesic adjunct, as well as a potentiator often used with analgesics like [codeine](/wiki/Codeine), [dihydrocodeine](/wiki/Dihydrocodeine), [hydrocodone](/wiki/Hydrocodone) and the like, is structurally related to the tricyclic antidepressants [[17]](#cite_note-17) {| class = wikitable |+ Pharmacokinetics of tramadol across the species<ref name = Zoo/> ! Species !! Half-life (h) for parent drug !! Half-life (h) for O-desmethyltramadol !! Maximum plasma concentration (ng/mL) for parent drug !! Maximum plasma concentration (ng/mL) for O-desmethyltramadol

|- | [Camel](/wiki/Camel) || 3.2 (IM), 1.3 (IV) || – || 0.44 (IV) || – |- | [Cat](/wiki/Cat) || 3.40 (oral), 2.23 (IV) || 4.82 (oral), 4.35 (IV) || 914 (oral), 1323 (IV) || 655 (oral), 366 (IV) |- | [Dog](/wiki/Dog) || 1.71 (oral), 1.80 (IV), 2.24 (rectal) || 2.18 (oral), 90-5000 (IV) || 1402.75 (oral) || 449.13 (oral), 90–350 (IV) |- | [Donkey](/wiki/Donkey) || 4.2 (oral), 1.5 (IV) || – || 2817 (oral) || – |- | [Goat](/wiki/Goat) || 2.67 (oral), 0.94 (IV) || – || 542.9 (oral) || – |- | [Horses](/wiki/Horses) || 1.29–1.53 (IV), 10.1 (oral) || 4 (oral) || 637 (IV), 256 (oral) || 47 (oral) |- | [Llama](/wiki/Llama) || 2.54 (IM), 2.12 (IV) || 7.73 (IM), 10.4 (IV) || 4036 (IV), 1360 (IM) || 158 (IV), 158 (IM) |}

## Pin cushion tree[[edit](/index.php?title=(none)&action=edit&section=21)]

In 2013, researchers reported that tramadol was found in relatively high concentrations (1%+) in the roots of the African [pin cushion tree](/wiki/Pin_cushion_tree) (*Nauclea latifolia*).<ref name = Nauc>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> In 2014, however, it was reported that the presence of tramadol in the tree roots was the result of tramadol having been administered to cattle by farmers in the region:<ref name = crosscont>[Template:Cite journal](/wiki/Template:Cite_journal)</ref> tramadol and its [metabolites](/wiki/Metabolites) were present in the animals' excreta, which contaminated the soil around the trees. Therefore, tramadol and its mammalian metabolites were found in tree roots in the far North of [Cameroon](/wiki/Cameroon), but not in the South where it is not administered to farm animals.<ref name = crosscont/>

A 2014 editorial in *Lab Times online* contested the notion that tramadol in tree roots was the result of anthropogenic contamination, stating that samples were taken from trees which grew in national parks, where livestock were forbidden; it also quoted researcher Michel de Waard, who stated that "thousands and thousands of tramadol-treated cattle sitting around a single tree and urinating there" would be required to produce the concentrations discovered.<ref name=LabTimes>[Who Really did it First? Nature or a Pharmacist?](http://www.labtimes.org/editorial/e_546.lasso), in *Lab Times online*; by Nicola Hunt; published September 22, 2014; retrieved November 21, 2015</ref>

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

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

* [Diabetic neuropathy](/wiki/Diabetic_neuropathy) [[64]](#cite_note-64)[[65]](#cite_note-65)\* [Antidepressant](/wiki/Antidepressant)[[66]](#cite_note-66)\* [postherpetic neuralgia](/wiki/Postherpetic_neuralgia) [[67]](#cite_note-67)[[68]](#cite_note-68)\* [Premature ejaculation](/wiki/Premature_ejaculation)[[69]](#cite_note-69)[[70]](#cite_note-70)\* [Obsessive-compulsive disorder](/wiki/Obsessive-compulsive_disorder)[[71]](#cite_note-71)

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

* [Indeloxazine](/wiki/Indeloxazine)
* [Venlafaxine](/wiki/Venlafaxine)

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

[Template:Reflist](/wiki/Template:Reflist)

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

* [Medline Plus – Patient Information](http://www.nlm.nih.gov/medlineplus/druginfo/meds/a695011.html) Medline Plus (A Service of the U.S. National Library of Medicine)
* [U.S. National Library of Medicine: Drug Information Portal – Tramadol](http://druginfo.nlm.nih.gov/drugportal/dpdirect.jsp?name=Tramadol)
* [Tramadol in the treatment of RSD](http://www.what-is-rsd.com/medication.html) (RSD = [Reflex Sympathetic Dystrophy](/wiki/Reflex_Sympathetic_Dystrophy))

[Template:Analgesics](/wiki/Template:Analgesics) [Template:Neuropathic pain and fibromyalgia pharmacotherapies](/wiki/Template:Neuropathic_pain_and_fibromyalgia_pharmacotherapies) [Template:Adrenergics](/wiki/Template:Adrenergics) [Template:Opioidergics](/wiki/Template:Opioidergics) [Template:Serotonergics](/wiki/Template:Serotonergics)

[Category:Analgesics](/wiki/Category:Analgesics) [Category:Euphoriants](/wiki/Category:Euphoriants) [Category:Amines](/wiki/Category:Amines) [Category:Cyclohexanols](/wiki/Category:Cyclohexanols) [Category:Mu-opioid agonists](/wiki/Category:Mu-opioid_agonists) [Category:Norepinephrine reuptake inhibitors](/wiki/Category:Norepinephrine_reuptake_inhibitors) [Category:5-HT2C antagonists](/wiki/Category:5-HT2C_antagonists) [Category:Phenol ethers](/wiki/Category:Phenol_ethers) [Category:Serotonin releasing agents](/wiki/Category:Serotonin_releasing_agents)